Association Between Epicardial Fat, HOMA-IR and Carotid Intima-media Thickness

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Received: 06/02/2011
Accepted: 09/21/2011

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ABSTRACT

Background
Epicardial fat is currently considered a real endocrine organ that can be easily determined by echocardiography, emerging as a novel parameter for the estimation of cardiometabolic risk.

Objective
To establish the association between epicardial fat, insulin resistance and carotid intima-media thickness.

Methods
The Instituto Nacional de Endocrinología and the Instituto Nacional de Cardiología y Cirugía Cardiovascular conducted a cross-sectional study on 239 patients with suspected disorders of carbohydrate metabolism. Clinical variables (age, gender, smoking habits, systolic and diastolic blood pressure), anthropometric measurements (waist circumference and body mass index), biochemical determinations (blood glucose, total cholesterol, HDL-C, LDL-C, triglycerides, fasting insulin level and HOMA-IR) and ultrasound measurements (carotid intima-media thickness) were assessed.

Results
A significant and independent association was found between blood glucose, epicardial fat and waist circumference, in that order, and HOMA-IR >2.6. Epicardial fat also showed a positive and significant correlation with fasting insulin levels (r=0.536; p=0.0001) and HOMA-IR (r=0.512; p=0.001). The correlation between epicardial fat and carotid intima-media thickness was greater in insulin resistant patients (r=0.523; p=0.0001), compared to patients with HOMA-IR <2.6 (r=0.173; p=0.029). Epicardial fat thickness ≥4.9 mm evidenced 85% sensitivity and 75% specificity to predict insulin resistance, with an area under the ROC curve of 0.815 (95% CI 0.759-0.871).

Conclusions
Epicardial fat had a significant an independent association with insulin resistance and a significant correlation with carotid intima-media thickness in the group of patients with HOMA-IR >2.6.

Rev Argent Cardiol 2012;80:222-229.

Key words > Epicardial Fat - Insulin Resistance - Atherosclerosis

Abbreviations >

EWC	Waist circumference	**HOMA-IR**	Homeostatic model assessment-insulin resistance
HDL-C	High density lipoprotein-cholesterol	**HT**	Hypertension
LDL-C	Low density lipoprotein-cholesterol	**BMI**	Body mass index
IMT	Intima-media thickness	**DBP**	Diastolic blood pressure
SBP	Systolic blood pressure		

The determination of epicardial fat by echocardiography has emerged as a novel parameter that can be easily measured for the estimation of cardiometabolic risk. (1) This visceral fat depot is currently considered a real endocrine organ which secretes proinflammatory and proatherogenic cytokines as tumor necrosis factor-alpha, interleukin-6, visfatin, leptin, omentin, plasminogen activator inhibitor 1, angiotensins and

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adipokines (adiponectin) with antiinflammatory and antiatherogenic effects. (2)

The correlation between epicardial fat, plasma insulin and adiponectin has suggested that this adipose tissue is strongly linked with insulin resistance, (3) and has an inverse association with insulin sensitivity (4) and with surrogate markers of insulin resistance such as HOMA-IR (homeostatic model assessment-insulin resistance). (5) Also, epicardial fat is related to the main anthropometric parameters of insulin resistance, as waist circumference (WC), for the estimation of visceral adipose tissue. (3)

Some investigations have suggested ethnic differences in the thickness and metabolic activity of epicardial fat. (6-8) The association between epicardial fat thickness and the presence of significant coronary artery disease in Hispanic patients (9) and of several markers of subclinical atherosclerosis in asymptomatic patients has been previously demonstrated. (10) However, the association among epicardial fat and HOMA-IR levels indicating insulin resistance, and intima-media thickness (IMT) in this group of patients, has not been well established in our region.

METHODS

Population study

Two hundred and thirty nine patients with suspected disorders of carbohydrate metabolism were included. They presented one or more of the following risk factors: 1) body mass index (BMI) > 27 (kg m2); 2) diabetes in first-degree relatives; 3) history of gestational diabetes and/or previous macrosomic baby; 4) history of glucose abnormalities; and, 5) hypertension with triglycerides > 150 mg/dL and high density lipoprotein-cholesterol (HDL-C) > 35 mg/dL. Patients were evaluated at the Instituto Nacional de Endocrinología from January 2009 to June 2010. The study was conducted following the recommendations of the Declaration of Helsinki and was approved by the Ethics Committee of our institution. All patients gave their informed consent before the beginning of the study.

Study design

Clinical variables, anthropometric measurements and biochemical determinations were evaluated by an endocrinologist at the Diabetes Center of the Instituto Nacional de Endocrinología. All the patients underwent transthoracic echocardiography and carotid artery ultrasound at the echocardiography laboratory of our institution within two weeks after the diagnosis was made. Patients with history of known cardiovascular disease, chronic kidney failure and those treated with statins were excluded from the study.

Protocol of the variables included in the study.

Clinical and anthropometric variables: age, gender, smoking habits, systolic blood pressure (SBP), diastolic blood pressure (DBP), weight, height, BMI and WC were recorded. Blood pressure was measured in the left arm using a mercury aneroid sphygmomanometer after a 5-minute rest period with the patient in the sitting position. Two measurements were taken in each patient with a difference of ten minutes, and the the average between them was the recorded value.

Biochemical variables: a 10-ml blood sample was withdrawn from the cubital vein and blood was transferred into three tubes: one with EDTA, another with heparin and a serum tube with gel separator. Fasting blood glucose, total cholesterol, HDL-C, low density lipoprotein-cholesterol (LDL-C) and triglycerides were determined. Blood glucose, total cholesterol and triglycerides were assayed using RapiGluco-Test, Colestest and Monotriglitest reagents, respectively, manufactured by the "Carlos J. Finlay" Enterprise of Biological Products, Havana, Cuba. An enzymatic colorimetric assay was used to measure blood glucose in an Eppendorf device and cholesterol and triglycerides were determined with a Hitachi 7170A (Tokyo, Japan) blood analyzer. HDL-C and LDL-C were measured using HDL-C Inmuno FS and LDL-C Select FS reagents, by in vitro serum or plasma quantitative determination in photometric systems (immunoturbidimetric assays) manufactured by DiaSys Diagnostic Systems GmbH, Holzheim, Germany). Insulin level was determined using a solid-phase radio-immunoassay kit (Coat-A.-Count Insulin, Diagnostic Products Corporation) provided by CENTIS with a sensitivity of 5 μUI/ml and a normal range of 5-35 μUI/ml. The intra- and inter-assay coefficients of variation were 6.2% and 7.1%, respectively. In our laboratory, the radioimmunoassay coefficient of variation for quality assessment varies between 6 and 9%, which is within the normal range for this type of radioimmunoassay.

The HOMA-IR was calculated using initial glucose and insulin values following the homeostatic model (HOMA) according to the following the equation: RI = [fasting insulin (μUI/ml) × fasting glucose (mmol/L)] / 22.5. The standardized reference value for the laboratory of the Instituto Nacional de Endocrinología is 2.6, validated by Arranz et al. (11, 12) so that higher values indicate insulin resistance.

Protocol of echocardiographic variables.

Epicardial fat: echocardiographic studies were performed with a Philips iE33 2006 echo system, version 2.0.1.420, and S5-1 phased array transducer (1.3-3.6 MHz) with harmonic imaging. The study was performed by two examiners meeting level III criteria of the American Society of Echocardiography, who were blinded to the patient's data.

Epicardial fat thickness was measured by two-dimensional echocardiography in the parasternal long-axis view at the level of the aortic valve plane (Figure 1 A) and in the parasternal short-axis view at the level of the papillary muscles (Figure 1 B). Epicardial fat thickness anterior to the right ventricle was determined as the average value obtained from the parasternal long-axis and short-axis views at end systole. Epicardial adipose tissue appears as an echo-free or a hyperechoic space between the echogenic line of the visceral pericardium and the epicardium of the right ventricular free wall. The correlation coefficients and inter and intraobserver variability of our echocardiography laboratory show good reproducibility, as previously reported. (9)

Carotid artery intima-media thickness: IMT measurements were obtained with the patient lying in the supine position and with the neck slightly rotated to the opposite side of the examination site. The artery was scanned in the longitudinal view with a 7.5 transducer positioned lateral and superior to the neck in the edge of the sternocleidomastoid muscle using the electrocardiogram signal to acquire end-diastolic vascular images viewed at a depth of 4 cm. IMT was measured in the common carotid artery along a 10-mm-long segment distal to the origin of the carotid artery bulb. Meas-

urements were performed using the QLAB semi-automated border detection software (Figure 2) and they were acquired if success in border detection was > 95%. Left and right common carotid artery IMT percentiles were established for age, race and gender according to the data provided by the Bogalusa Heart Study (13) and the MESA study (Multi-Ethnic Study of Atherosclerosis) (14). If discrepant percentiles were found between both carotid arteries, the highest percentile value was assigned.

Statistical Analysis

Statistical analysis was performed using SPSS 13.0 statistical package (SPSS Inc., Chicago, III, USA). The distribution and the association of the general characteristics of the study population were determined by gender. The categorical variables were expressed as absolute values and percentages and continuous variables as means and standard deviations. For univariate analysis, the chi square test was used to compare categorical variables and Student´s t test for continuous variables. A p value < 0.05 was considered statistically significant.

A multivariate analysis was performed among clinical, anthropometric, biochemical and ultrasound variables and HOMA-IR > 2.6, using binary logistic regression for each variable that in univariate analysis had a p value < 0.20 with respect to this surrogate marker of insulin resistance, to determine its independence from the other factors of cardiometabolic risk included in the study. The odds ratio, with its corresponding 95% CI was also calculated. The area under the ROC curve was used to determine the cutoff value of epicardial fat with the best sensitivity and specificity to predict insulin resistance. The ROC curves were compared with the chi-square test for homogeneity using EPIDAT 3.1 software.

Pearson's correlation coefficient was used to determine the correlation between epicardial fat with fasting insulin levels, HOMA-IR and carotid IMT according to the presence or absence of insulin resistance. A significant association between variables was considered for p < 0.05.

RESULTS

General characteristics of the study population

Table 1 shows the general characteristics of the study population.

Two hundred and thirty nine patients with suspected carbohydrate metabolism disorders were included in the study: 143 (59.8%) women, patient mean age was 54.7 ± 8.9 vs. 55.5 ± 9.4 for women and men, respectively, 79 (33.1%) presented insulin resistance and 84 (35.7%) had IMT in the ≥ 75 percentile.

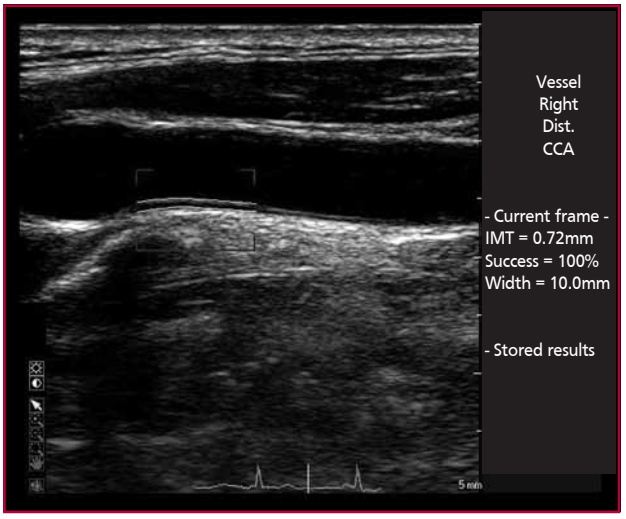

Fig. 2. Measurement of intima-media thickness. Lines were drawn with the QLAB semi-automated border detection software.

Epicardial fat thickness varied from 1.0 mm to a maximum of 12.5 mm (mean 4.7 mm ± 2.1 mm.)

Of note, mean LDL-C and triglyceride levels in the study population were above normal reference values.

Clinical, anthropometric, biochemical and echocardiographic variables according to the presence of insulin resistance (Table 2)

Univariate analysis demonstrated that BMI, WC, blood glucose levels, triglycerides, epicardial fat and carotid IMT, in that order, had a significant association with the presence of insulin resistance. Ultimately, blood glucose, epicardial fat and WC showed a significant and independent association with HOMA-IR > 2.6. Epicardial fat ≥ 4.9 mm had a sensitivity of 85% and a specificity of 75% to predict insulin resistance, with

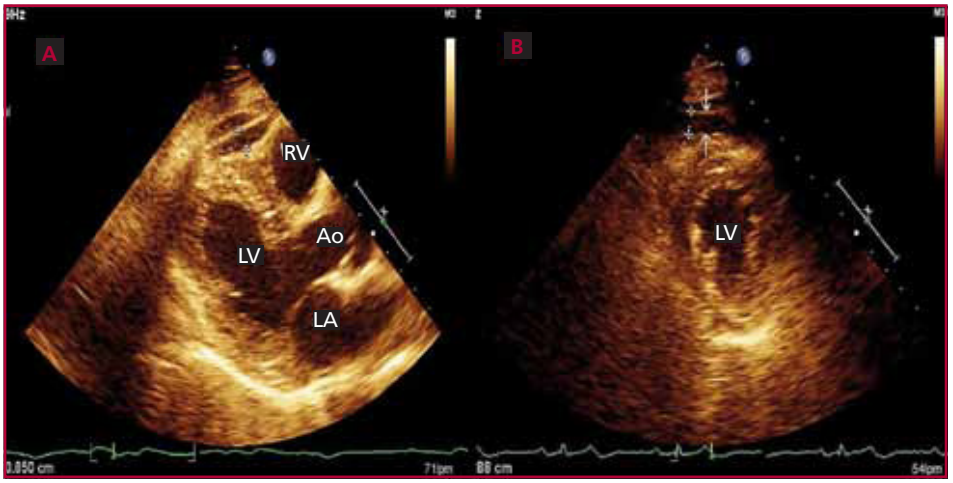

Fig. 1. Echocardiographic assessment of epicardial fat. **A.** Parasternal long-axis view at the level of the aortic valve plane. **B.** Parasternal short-axis view at the level of the papillary muscles Epicardial fat (arrows). Ao: Aorta. LV: Left ventricle. RV: Right ventricle. LA: Left atrium.

an area under the ROC curve of 0.840 (95% CI 0.785-0.896) that was significantly higher than that of WC [0.776, 95% CI 0.710-0.841; p = 0.039] (Figure 3).

Correlation between epicardial fat with insulin resistance and carotid IMT

Epicardial fat showed a positive and significant correlation with fasting insulin levels (r = 0.536; p = 0.0001) (Figure 4) and HOMA-IR (r = 0.512; p = 0.001). In addition, the correlation between epicardial fat and carotid IMT was greater in insulin resistant patients (r = 0.523; p = 0.0001) (Figure 5 A), compared to patients with HOMA-IR < 2.6 (r = 0.173; p = 0.029) (Figure 5 B).

DISCUSSION

The most relevant findings of our study were the following: 1) epicardial fat showed a positive and significant correlation with fasting insulin levels and HOMA-IR, and, 2) the strongest association with carotid IMT was seen in the group of insulin resistant patients.

Epicardial fat and insulin resistance

Epicardial fat is made up of adipocytes and macrophages, both with secreting properties, and significant autocrine, paracrine and endocrine functions. (15) The role of adipokines as regulators of insulin sensitivity has been recently demonstrated. Tumor necrosis factor-alpha, interleukin-6 and leptin have been recognized as the most prominent members of this family of proinflammatory cytokines produced by epicardial fat, contributing to insulin resistance. (16) Similarly, the levels of adiponectins are typically reduced in insulin-resistant patients (17) and this reduction behaves as a predictor of diabetes and fatty liver. (18)

In a study including 30 obese patients, Iacobellis et al. were the first to demonstrate a significant correlation between epicardial fat thickness and fasting insulin (r = 0.59; p = 0.01) and insulin at 120 minutes (r = 0.45; p = 0.03). (5) In a subsequent study, this author reported a proportional and significant increase in epicardial fat thickness in insulin sensitive, insulin resistant and highly insulin resistant patients (5.4 mm vs. 9.5 mm vs. 11.0 mm; p < 0.001). (4)

Aydin et al. studied 50 patients with metabolic syndrome to demonstrate the association between endothelial function and epicardial fat. They found a significant correlation between epicardial fat and fasting blood glucose (r = 0.307; p = 0.020), fasting insulin (r = 0.376; p = 0.002) levels, HOMA-IR values (r = 0.370; p = 0.002) and flow-mediated dilatation (R2 = 0.247; p = 0.001), an ultrasound marker of early stages of atherosclerosis. (19)

Epicardial fat has also shown a significant association with the presence of metabolic syndrome. Ahn et al. demonstrated a significant correlation between epicardial fat and fasting blood glucose, fasting insulin and HOMA-IR values. They also showed that epicardial fat thickness was significantly greater in the nondiabetic group with metabolic syndrome (3.5 vs. 1.6 mm; p < 0.001). (20) A recent study reported similar results with significant greater values of epicardial fat in patients with type 1 diabetes and metabolic syndrome (6.15 ± 0.34 mm vs. 4.96 ± 0.25 mm; p = 0.006). (21)

The sensitivity and specificity of epicardial fat to predict insulin resistance reported by some authors are similar to our findings; however, we used lower cutoff

Table 1. General characteristics of the study population

Variables	Female n = 143	Male n = 96	Total n = 239	p
Age, years	54.7 ± 8.9	55.5 ± 9.4	53.4 ± 8.9	0.535
Smoking habits, n (%)	31 (21.7%)	21 (21.9%)	52 (21.8%)	0.547
SBP, mm Hg	128 ± 18.9	135 ± 18.8	130.9 ± 19	0.006*
DBP, mm Hg	79 ± 13.3	82 ± 12.2	80.2 ± 13	0.079
BMI (kg/m2)	27.9 ± 6.6	27.5 ± 4.3	27.7 ± 5.8	0.547
Waist, cm	89.6 ± 12	97.4 ± 12	92.7 ± 13	0.000*
Glucose, mg/dL	87 ± 38	86 ± 25	86.3 ± 34	0.928
Cholesterol, mg/dL	224 ± 50	201 ± 43	216 ± 50	0.001*
HDL-C, mg/dL	56 ± 15	47 ± 23	53 ± 19	0.001*
LDL-C, mg/dL	124 ± 35	114 ± 31	3.1 ± 0.9	0.027*
Triglycerides, mg/dL	171 ± 80	185 ± 115	2.01 ± 1.1	0.261
Uric acid, mg/dL	5.16 ± 1.7	5.26 ± 1.7	306.2 ± 98.9	0.671
Blood insulin, pmol/L	72 ± 40	67 ± 35	70 ± 38	0.364
HOMA-IR	2.2 ± 2.2	2.2 ± 1.6	2.2 ± 1.98	0.747
IMT, mm	0.71 ± 0.13	0.75 ± 0.16	0.72 ± 0.14	0.051
Epicardial fat, mm	4.89 ± 2.1	4.39 ± 2.2	4.7 ± 2.1	0.081

SBP: Systolic blood pressure. DBP: Diastolic blood pressure. BMI: Body mass index. HDL-C: High density lipoprotein-cholesterol. LDL-C: Low density lipoprotein-cholesterol. IMT: Intima-media thickness. *Significant association in univariate analysis.

Table 2. Clinical, anthropometric, biochemical and echocardiographic variables according to the presence of insulin resistance defined by HOMA-IR.

Variables	HOMA-IR ≥ 2.6 n = 79	HOMA-IR < 2.6 n = 160	Odds ratio (95% CI)	p*	Odds ratio (95% CI)	p**
Age, years	55.1 ± 8.8	55.0 ± 9.3	_	0.971	_	_
Male, n (%)	31 (39.2%)	65 (40.6%)	0.96 (0.66-1.40)†	0.467	_	_
Female, n (%)	48 (60.8%)	95 (59.4%)				
Smoking habits, n (%)	21 (26.6%)	29 (18.1%)	1.67 (0.88-3.17)	0.082	1.01 (0.99-1.27)	0.546
SBP, mm Hg	133 ± 19	129 ± 19	_	0.143	0.65 (0.29-1.44)	0.289
DBP, mm Hg	82 ± 13	80 ± 13	_	0.212	_	
BMI (kg/m2)	29.7 ± 5.9	26.7 ± 5.5	_	< 0.001*	0.96 (0.89-1.02)	0.183
Waist, cm	98.8 ± 13	89.6 ± 11	_	< 0.001*	1.96 (1.93-1.99)	0.012**
Glucose, mg/dL	104 ± 42	78 ± 29	_	< 0.001*	1.41 (1.29-1.58)	0.000**
Cholesterol, mg/dL	216 ± 46	214 ± 50	_	0.720	_	_
HDL-C, mg/dL	54 ± 19	49 ± 19	_	0.066	1.27 (0.78-2.78)	0.233
LDL-C, mg/dL	118 ± 35	121 ± 35	_	0.507	_	_
Triglycerides, mg/dL	206 ± 115	163 ± 80	_	0.001*	1.35 (0.33-5.53)	0.675
Uric acid, mg/dL	5.3 ± 1.7	5.0 ± 1.7	_	0.293	_	_
Epicardial fat, mm	5.3 ± 2.3	4.3 ± 2.1	_	0.001*	1.82 (1.71-1.96)	0.011**
carotid IMT, mm	0.76 ± 0.17	0.71 ± 0.13	_	0.018*	1.38 (1.34-4.24)	0.430

SBP: Systolic blood pressure. DBP: Diastolic blood pressure. BMI: Body mass index. HDL-C: High density lipoprotein-cholesterol. LDL-C: Low density lipoprotein-cholesterol. IMT: Intima-media thickness. * Significant association in univariate analysis. **Significant association in multivariate analysis.

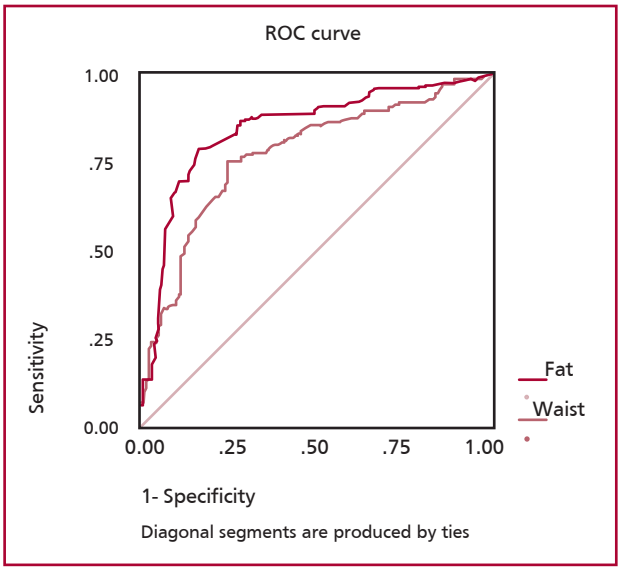

Fig. 3. Area under the curve for epicardial fat and waist circumference to predict insulin resistance.

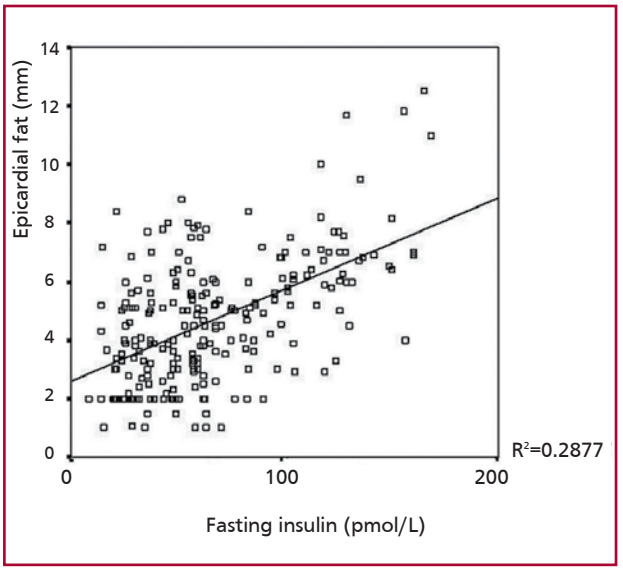

Fig. 4. Correlation between epicardial fat and fasting insulin values.

values compared to other studies. (4, 22) Iacobellis et al. reported that epicardial fat thickness > 9.5 mm in men and 7.5 mm in women had a sensitivity of 85.0% and 82.0% and a specificity of 63.0% and 62.0%, respectively, to predict insulin resistance [area under the curve 0.792 (95% CI 0.725-0,.848)]. In that study, epicardial fat ranged between 1.1 mm and 22.6 mm. (4) In another study conducted in obese children (mean age 10.2 ± 2.5 years), the area under the curve was 0.750 ± 0.06 (p = 0.001) for epicardial fat thickness >

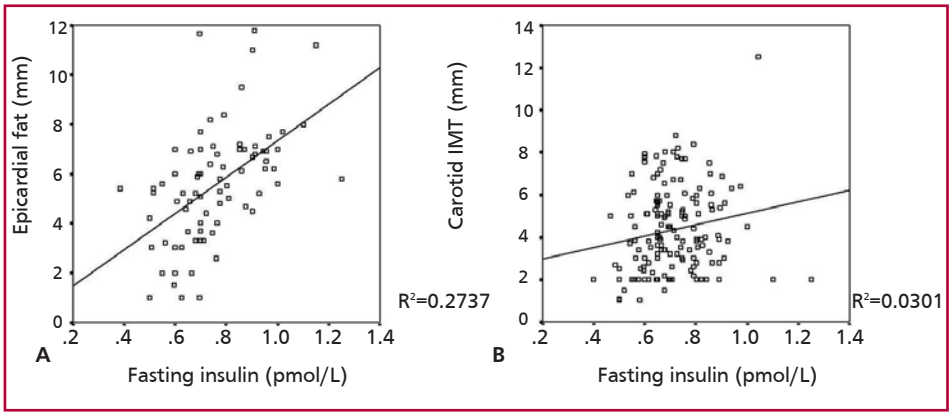

Fig. 5. Correlation between epicardial fat and carotid intima-media thickness according to the presence or absence of insulin resistance.

4.1 mm, with a sensitivity of 90% and a specificity of 61% to predict insulin resistance. (22)

Other studies have reported greater mean values of epicardial fat thickness [(9.87 mm, (3) 8.0 mm, (23) 6.16 mm (19) and 6.15 mm (21)] in patients with insulin resistance or metabolic syndrome than those in the present study (5.3 mm). Interestingly, some investigations have suggested ethnic differences in epicardial fat thickness. This adipose depot seems to be lower in Hispanic patients, as reported by Alexopoulos et al. who found that the volume of epicardial fat measured by computed tomography was smaller in Hispanics compared to other ethnic groups, even blacks (Caucasians 96 ± 44 ml vs. Asians 71 ± 32 ml vs. blacks 56 ± 28 ml vs. Hispanics 54 ± 17 ml; $p < 0.001$). (24)

In the first study demonstrating a significant association between epicardial fat and the presence of major coronary artery disease in Hispanic patients, the mean values of epicardial fat were also lower than those reported in the literature for this group of patients. (9)

Epicardial fat and carotid IMT

Iacobellis et al. were also the first authors to demonstrate a significant correlation between epicardial fat and carotid IMT. In a study including 60 HIV-infected patients with antiretroviral therapy-induced lipodystrophy, they reported that epicardial fat thickness and carotid IMT were significantly greater in the group of patients with metabolic syndrome and lipodistrophy compared to those without lipodistrophy (8.0 vs. 6.5 mm, $p < 0.01$ and 0.71 vs. 0.66 mm, $p < 0.01$, respectively). In that study, epicardial fat showed a significant correlation with fasting insulin levels ($r = 0.65$; $p < 0.01$). (23)

Abaci et al. demonstrated a significant correlation between epicardial fat and carotid IMT in obese children ($r = 0.343$; $p = 0.02$). (22) In a study including 459 hypertensive patients, epicardial fat > 7 mm was significantly associated with greater carotid IMT and parameters of arterial stiffness compared to those with epicardial fat ≤ 7 mm. (25) Finally, Rego et al. examined 300 asymptomatic subjects and found that epicardial fat had a significant association with carotid IMT, coronary artery calcification, increased ApoB/ApoA1 ratio and cardiovascular risk according to the Framingham score. (10)

Several studies have demonstrated that the leptin/adiponectin ratio (both adipokines related with insulin resistance) is significantly associated with carotid IMT (26-28) and other ultrasound markers of atherosclerosis, as flow-mediated dilatation and carotid artery distensibility. (27) Similarly, other studies have reported that increased insulin levels seem to be earlier predictors of atherogenic changes than hyperglycemia. (29) Based on these findings, we may assume that a significant increase of epicardial fat in patients with insulin resistance and its correlation with fasting glucose levels and HOMA-IR might explain the higher correlation between epicardial fat and carotid IMT in insulin-resistant patients.

The cross-sectional design of the study and the use of HOMA-IR as a surrogate marker of insulin resistance are limitations of this study. Previous studies have shown similar characteristics. However, further prospective studies are necessary to assess the ability of epicardial fat thickness to predict cardiovascular risk or how epicardial fat is modified in relation to changes in cardiometabolic parameters during follow-up. (2) According to the International Diabetes Federation 2005 Metabolic Syndrome Consensus, insulin resistance can be determined by the hyperinsulinemic-euglycemic clamp (gold standard). However, this is an invasive and complex procedure for the clinical practice. Instead, we used the HOMA-IR index, a simple, low-cost mathematical model, suitable for population-based studies. (30)

CONCLUSIONS

The echocardiographic determination of epicardial fat can be a useful prognostic tool to assess cardiometabolic risk stratification, as a significant an independent association with insulin resistance and a significant correlation with carotid intima-media thickness was found in the group of patients with HOMA-IR > 2.6. Further prospective and multiethnic studies with larger samples are necessary to validate these results.

RESUMEN

Grasa epicárdica y su asociación con el HOMA-IR y el grosor íntima-media carotídeo

Introducción
La grasa epicárdica se considera actualmente como un verdadero órgano endocrino y su determinación ecocardiográfica ha surgido como un nuevo parámetro de fácil adquisición en la evaluación del riesgo cardiometabólico.

Objetivo
Determinar la asociación entre la grasa epicárdica, la presencia de insulinorresistencia y el grosor íntima-media carotídeo.

Material y métodos
Se realizó un estudio transversal en 239 pacientes con sospecha de trastornos en el metabolismo de los carbohidratos en colaboración entre el Instituto Nacional de Endocrinología y el Instituto Nacional de Cardiología y Cirugía Cardiovascular. Se incluyeron variables clínicas (edad, sexo, antecedentes de tabaquismo, presión arterial sistólica y diastólica), antropométricas (circunferencia de la cintura e índice de masa corporal), bioquímicas (glucemia, colesterol total, C-HDL, C-LDL, triglicéridos, insulina en ayunas y HOMA-IR) y ultrasonográficas (grosor íntima-media carotídeo).

Resultados
La glucemia, la grasa epicárdica y la circunferencia de la cintura fueron las variables que mostraron, en ese orden, una asociación significativa e independiente con la presencia de un HOMA-IR > 2,6. La grasa epicárdica mostró también una correlación positiva y significativa con los niveles de insulinemia en ayunas ($r = 0,536$; $p = 0,0001$) y con el HOMA-IR ($r = 0,512$; $p = 0,001$). La correlación entre la grasa epicárdica y el grosor íntima-media carotídeo fue superior en los pacientes insulinorresistentes ($r = 0,523$; $p = 0,0001$), en comparación con los pacientes con valores de HOMA-IR < 2,6 ($r = 0,173$; $p = 0,029$). La grasa epicárdica ≥ 4,9 mm tuvo una sensibilidad del 85% y una especificidad del 75% en la predicción de insulinorresistencia, con un área bajo la curva ROC de 0,815 [IC 95% (0,759-0,871)].

Conclusiones
La grasa epicárdica mostró una asociación significativa e independiente con la presencia de insulinorresistencia y una correlación significativa con el grosor íntima-media carotídeo en el grupo de pacientes con HOMA-IR > 2,6.

Palabras clave > Grasa epicárdica - Resistencia a la insulina - Aterosclerosis

REFERENCES

1. MacGavock J, Víctor RU, Roger H, Szczepaniak LS. Adiposity of the heart, Revisited. Ann Int Med 2006;114:517-24.
2. Iacobellis G, Willens HJ. Echocardiographic epicardial fat: a review of research and clinical applications. J Am Soc Echocardiogr 2009;22:1417-8.
3. Iacobellis G, Ribaudo MC, Assael F, Vecci E, Tiberti C, Zappaterreno A, 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.
4. Iacobellis G, Willens HJ, Barbaro G, Sharman AM. Threshold values of high risk echocardiographic epicardial fat thickness. Obesity (Silver Spring) 2008;16:887-92.
5. Iacobellis G, Leonetti F. Epicardial adipose tissue and insulin resistance in obese subjects. J Clin Endocrinol Metab 2005;90:6300-2.
6. Howard JW, Gómez-Marín O, Chirinos JA, Goldberg R, Lowery MH, Iacobellis G. Comparison of epicardial and pericardial fat thickness assessed by echocardiography in African American and non-Hispanic white men: a pilot study. Ethn Dis 2008;18:311-6.
7. Alexopoulos N, McLean DS, Janik M, Arepalli ChD, Stillman AE, Raggi P. Epicardial adipose tissue and coronary artery plaque characteristics. Atherosclerosis 2010;210:150-4.
8. Divers J, Wagenknecht LE, Bowden DW, Carr J, Hightower RC, Register TC, et al. Ethnic differences in the relationship between pericardial adipose tissue and coronary artery calcified plaque: African-American-Diabetes Heart Study. J Clin Endocrinol Metab 2010;95:5382-9.
9. Mustelier JV, Rego JO, González GA, Sarmiento JC, Riverón BV. Echocardiographic parameters of epicardial fat deposition and its relation to coronary artery disease. Arq Bras Cardiol 2011;97:122-9.
10. Rego JO, Iacobellis G, Sarmientos JC, Mustelier JV, Aquiles EW, Rodríguez VM, et al. Epicardial fat thickness correlates with ApoB/ApoA1 ratio, coronary calcium and carotid intima media thickness in asymptomatic subjects. Int J Cardiol 2011;151:234-36.
11. Arranz C, Álvarez A, Perich P, González R. Relación de la sensibilidad a la insulina determinada con diferentes índices con el síndrome metabólico en hombres con glicemia en ayunas normal. Rev Asociación Latinoam Diabetes 2007;15:120.
12. Arranz C, González R, Álvarez A, Rodríguez B, Reyes A. Criterios de referencia para los indicadores de secreción de insulina y de los parámetros lipídicos en una población mixta hospitalaria. Rev Cubana Endocrinol 2010;21:1-12.
13. Tzou WS, Douglas PS, Srinivasan SR, Bond MG, Tang R, Chen W, et al. Distribution and predictors of carotid artery intima-media thickness in young adults: the Bogalusa Heart Study. Prev Cardiol 2007;10:181-9.
14. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults: Cardiovascular Health Study Collaborative Research Group. N Engl J Med 1999;340:14-22.
15. Matsuzawa Y. Therapy insight: adipocytokines in metabolic syndrome and related cardiovascular disease. Nat Clin Pract Cardiovasc Med 2006;3:35-42.
16. Mazurek T, Zhang L, Zalewski A, Mannion JD, Diehl JT, Arafat H, et al. Human epicardial adipose tissue is a source of inflammatory mediators. Circulation 2003;108:2460-6.
17. Abbasi F, Chu JW, Lamendola C, McLaughlin T, Hayden J, Reaven GM, et al. Discrimination between obesity and insulin resistance in the relationship with adiponectin. Diabetes 2004;53:585-90.
18. Bajaj M, Suraamornkul S, Piper P, Hardies LJ, Glass L, Cersosimo E, et al. Decreased plasma adiponectin concentrations are closely related to hepatic fat content and hepatic insulin resistance in pioglitazone-treated type 2 diabetic patients. J Clin Endocrinol Metab 2004;89:200-6.
19. Aydin H, Toprak A, Deyneli O, Yazici D, Tarçin Ö, Sancak S, et al. Epicardial fat tissue thickness correlates with endothelial dysfunction and other cardiovascular risk factors in patients with metabolic syndromes. Metabolic Syndrome and Related Disorders 2010;8:229-34.
20. Ahn GS, Lim HS, Joe DY, Kang SJ, Choi BJ, Choi SY, et al. Relationship of epicardial adipose tissue by echocardiography to coronary artery disease. Heart 2008;94:e7.
21. Momesso DP, Bussade I, Epifanio MA, Schettino CD, Russo LA, Kupfer R. Increased epicardial adipose tissue in type 1 diabetes is associated with central obesity and metabolic syndrome. Diabetes Res Clin Pract 2011;91:47-53.
22. Abaci A, Tascilar ME, Saritas T, Yozgat Y, Yesilkaya E, Kilic A, et al. Threshold value of subepicardial adipose tissue to detect insulin resistance in obese children. Int J Obes 2009;33:440-6.
23. Iacobellis G, Pellicelli AM, Sharma AM, Grisorio B, Barbarini G, Barbaro G. Relation of subepicardial adipose tissue to carotid intima-media thickness in patients with human immunodeficiency virus. Am J Cardiol 2007;99:1470-2.
24. Alexopoulos N, McLean DS, Janik M, Arepalli CD, Stillman AE, Raggi P. Epicardial adipose tissue and coronary artery plaque characteristics. Atherosclerosis 2010;210:150-4.
25. Natale F, Tedesco MA, Mocerino R, de Simone V, Di Marco GM, Aronne L, et al. Visceral adiposity and arterial stiffness: echocardiographic epicardial fat thickness reflects, better than waist circumference, carotid arterial stiffness in a large population of

hypertensives. Eur J Echocardiogr 2009;10:549-55.
26. Norata GD, Raselli S, Grigore L, Garlaschelli K, Dozio E, Magni P, et al. Leptin:adiponectin ratio is an independent predictor of intima media thickness of the common carotid artery. Stroke 2007;38:2844-6.
27. Saarikoski LA, Huupponen RK, Viikari JS, Marniemi J, Juonala M, Kähönen M, et al. Adiponectin is related with carotid artery intima-media thickness and brachial flow-mediated dilatation in young adults the Cardiovascular Risk in Young Finns Study. Ann Med 2010;42:603-11.
28. Takamura N, Hayashida N, Hagane K, Kadota K, Yamasaki H, Abiru N, et al. Leptin to high-molecular-weight adiponectin ratio is independently correlated with carotid intima-media thickness in men, but not in women. Biomarkers 2010;15:340-4.
29. Fang J, Zhang JP, Luo CX, Yu XM, Lu LQ. Carotid intima-media thickness in childhood and adolescent obesity relations to abdominal obesity, high triglyceride level and insulin resistance. Int J Med Sci 2010;7:278-83.
30. Ascaso JF, González-Santos P, Mijares AH, Rojas AM, Marín LM, Núñez-Cortés JM, et al. Diagnóstico de síndrome metabólico. Adecuación de los criterios diagnósticos en nuestro medio. Recomendaciones del foro HDL. Resumen ejecutivo. Rev Clin Esp 2006;206:576-82.