Short Reports

Correlation between epicardial fat thickness with intima–media thickness and ankle–brachial index in patients with metabolic syndrome

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ABSTRACT

Background. An increase in epicardial fat thickness (EFT) has been associated with increased cardiovascular risk and the development of atherosclerosis. Transthoracic echocardiography provides a reliable measurement of EFT. We evaluated the relationship of EFT with carotid intima–media thickness (CIMT) and ankle–brachial index (ABI), in patients with metabolic syndrome.

Methods. We assessed 80 patients with metabolic syndrome who underwent echocardiography; EFT was measured by two cardiologists. The CIMT (B-mode colour imaging of extracranial carotid arteries using high-resolution ultrasound) was also measured by a certified ultrasonographer, and ABI was measured by the main researcher.

Results. We did not find any correlation between ABI with EFT ($r=0.0103$, $p=0.93$) or with CIMT ($r=-0.1625$, $p=0.15$). However, we found a significant correlation between EFT and CIMT ($r=0.2718$, $r^2=0.074$, $p=0.015$). When we evaluated the risk for a CIMT ≥ 0.9 mm in patients with an EFT ≥ 3 mm, we found a statistically significant association ($p=0.039$). Interestingly, only 1 patient with an EFT < 3 mm had a CIMT ≥ 0.9 mm.

Conclusion. We found that the EFT correlates with CIMT in patients with metabolic syndrome, which explains, at least in part, the higher risk of atherosclerosis in them. Measurement of EFT should be part of the cardiovascular risk evaluation in patients with metabolic syndrome.

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INTRODUCTION

Metabolic syndrome clusters several abnormalities that had been considered as risk factors for cardiovascular disease. In fact, participants with metabolic syndrome have a higher risk for the development of diabetes mellitus and coronary artery disease (CAD).[1]

The increase in carotid intima–media thickness (CIMT), measured by high-resolution ultrasonography has been directly associated with atherosclerosis, myocardial infarction and stroke. High-resolution B-mode ultrasonography provides a non-invasive method that can detect an increase in arterial wall thickness, and may be useful as a screening test for the evaluation of the risk of CAD.[2]

Ankle–brachial index (ABI) is the ratio of the ankle and brachial systolic pressure; it is a non-invasive, office measurement method for diagnosing peripheral artery disease (PAD).[3]

A low ABI (<0.9) could be considered as a predictor of cardiovascular and cerebrovascular disease. Patients with an ABI <0.9 have a significantly reduced survival compared to those with normal ABI. There is an increase of 10.2% in the relative risk of cardiovascular events and mortality by every 0.1 reduction in the ABI.[4]

Epicardial adipose tissue is true visceral fat deposited between the myocardium and pericardium; physiological functions of epicardial fat include mechanical protection of the myocardium, and to be a source of energy and anti-atherogenic adipokines such as adiponectin and omentin. Due to their contiguity (because of the absence of fascia) and as the myocardium and epicardial fat share the same microcirculation, both tissues interact through paracrine and vasocrine actions of those adipokines.[5]

An increase in epicardial fat thickness (EFT) has been associated with the release of pro-inflammatory and pro-atherogenic adipokines such as resistin and tumour necrosis factor α, and with the development of atherosclerosis.[6] An EFT >3 mm has been associated with metabolic syndrome in the Mexican population.[7]

The measurement of EFT on the free wall of the right ventricle, as described by Iacobellis *et al.*, provides a simple, cheap and readily available assessment of EFT.[5,6] EFT has been associated with cardiovascular disease. However, little is known about how EFT is related to atherosclerosis when compared with other clinical markers of vascular disease. We evaluated the relationship of EFT with CIMT and ABI in patients with metabolic syndrome.

METHODS

We included 80 consecutive patients with metabolic syndrome (in accordance with the International Diabetes Federation criteria),[8] who underwent an echocardiographic study in our facility. In all of them, EFT was measured. EFT was identified as the echo-free space between the outer wall of the myocardium and the visceral layer of the pericardium. It was measured on the free wall of the right ventricle, perpendicularly at end-systole from the parasternal long-axis views of three cardiac cycles by standard transthoracic 2-dimensional echocardiography, as described by Iacobellis *et al.*,[5] with an Aloka Alfa six equipment (Japan) using a 3.5 MHz transducer, by two cardiologists who were unaware of the clinical data.

B-mode colour imaging of extracranial carotid arteries was done using high-resolution ultrasound (ESAUTE MEGAGP, Italy) equipped with a 10-MHz linear transducer. Patients were evaluated lying in the supine position with hyperextension of the neck. The distal wall of the common and internal carotid arteries was measured. Measurements were done at the end of diastole, and by the same certified ultrasonographer who was blinded to the clinical data.

For the measurement of ABI, patients were placed in the supine position, with the arms and legs at the same level as the heart, for a minimum of 5 minutes before any measurement. The systolic blood pressure was measured in the right and left posterior tibial arteries and right and left brachial arteries, respectively using a standard mercury sphygmomanometer and a hand-held Doppler instrument (5 MHz, Summit Doppler L250, Life Dop., EUA) by the main researcher. The higher ankle systolic pressure was divided by the higher brachial systolic pressure.

In all patients, serum glucose (glucose oxidase), creatinine (JAFFE), low-density lipoprotein, high-density lipoprotein (CHODPAP) and triglycerides (Triglyceride-pap) were measured. All venous samples were collected in the morning after 12 hours overnight fast.

Patients with any of the following diagnoses were excluded from the study: decompensated diabetes mellitus (glucose ≥250 mg/ml); heart, hepatic or renal failure; evidence of valvular heart disease, heart block or cardiac arrhythmia, acute coronary syndrome or cerebrovascular disease 6 months before the study. Those with autoimmune disease, pregnancy, malignancy and alcohol or psychotropic drug abuse were also excluded.

The study was conducted with the approval of the Research and Ethics Committee of our hospital, in accordance with the Declaration of Helsinki (register number 208/010/014/16). Participants gave written informed consent before their inclusion in the study.

Statistical analysis

Data are presented as mean (standard deviation). The correlation between EFT and CIMT and ABI was done with the Pearson coefficient test, whereas the association between EFT and CIMT was evaluated with the Fisher's exact test; a p value of <0.05 was considered statistically significant.

RESULTS

The baseline characteristics of our patients are shown in Table I. We did not find any correlation between ABI and EFT (r=0.0103, p=0.93) or with CIMT (r=–0.1625, p=0.15). However, we found a significant correlation between EFT and CIMT (r=0.2718, r^2=0.074, p=0.015; Fig. 1).

When we evaluated the risk for a CIMT ≥0.9 mm in patients with an EFT ≥3 mm, we found a statistically significant association (p=0.039). Interestingly, only 1 patient with an EFT <3 mm had a CIMT ≥0.9 mm (Table II).

TABLE I. Baseline characteristics of patients

Characteristic	Value*
Age (years)	50.6 (9.7)
Sex (male/female)	24/56
Body mass index	32.2 (6.9)
Waist circumference (cm)	102.6 (13.1)
Blood pressure (mmHg)	125/82 (14/8)
Epicardial fat thickness (mm)	5.2 (1.7)
Intima–media thickness (mm)	0.98 (0.2)
Ankle–brachial index	0.89 (0.14)
Glycaemia (mg/dl)	135.9 (37.5)
Triglycerides (mg/dl)	349.5 (206.0)
High-density lipoproteins (mg/dl)	40.9 (8.8)
Low-density lipoproteins (mg/dl)	126.1 (32.8)
Uric acid (mg/dl)	6.3 (1.6)

* All values are mean (SD) except sex which is a number

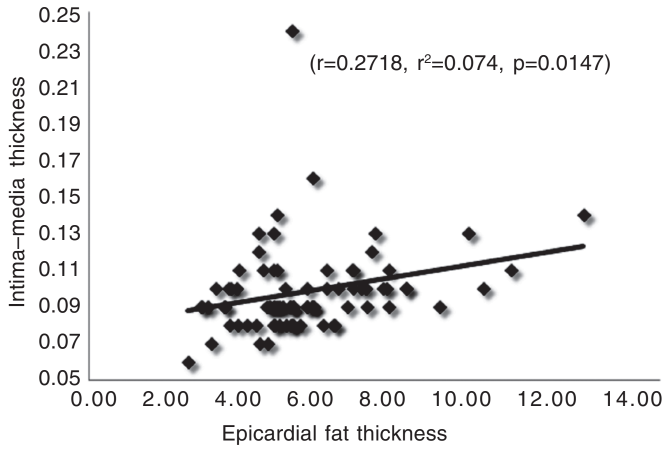

FIG 1. Correlation between epicardial fat thickness and intima–media thickness

TABLE II. Distribution of patients according to epicardial fat thickness (EFT) and carotid intima–media thickness (CIMT)

CIMT value	EFT ≥3 mm	EFT <3 mm
≥0.9 mm	60 patients	1 patient
<0.9 mm	16 patients	3 patients

DISCUSSION

We found that EFT correlates with CIMT but not with ABI in patients with metabolic syndrome. Epicardial fat is a metabolically active tissue that secretes adipokines that can affect the myocardium and coronary vessels through several pathways, although its pathophysiological roles are not well understood, EFT has emerged as a new risk factor that may play a role in the development of atherosclerosis; this fact is supported by our findings.

The increase in CIMT, measured by high-resolution ultrasonography, provides a non-invasive method that can detect atherosclerosis as an increase in arterial wall thickness before a reduction in lumen diameter occurs.[9] Interestingly, the American Association of Clinical Endocrinologists and the American College of Endocrinology Guidelines for Management of Dyslipidemia and Prevention of Cardiovascular Disease recommend considering the use of CIMT to refine risk stratification to determine the need for more aggressive atherosclerotic cardiovascular disease preventive strategies (recommendation Grade B).[10]

The ABI is used for the non-invasive diagnosis of lower-extremity PAD. However, the ABI is also recognized as an indicator of atherosclerosis and can serve as a prognostic marker for cardiovascular risk.[11]

Even though both CIMT and ABI are markers of atherosclerosis, we found correlation only between EFT and CIMT, but not with ABI, we do not have an explanation for this fact, but it may be secondary to a greater disturbed flow in carotid vessels,[9] which leads to an earlier beginning of the atherosclerotic process in that vascular territory than in lower extremity arteries. This fact requires experimental corroboration. Laguna *et al*. did not find increased CIMT in patients with PAD.[12]

Our results are similar to those of Yi *et al*., who found that patients with ectopic liver fat accumulation have higher CIMT and increased risk of atherosclerosis;[13] moreover, with those of Acele *et al*., who found an association between EFT and thoracic aortic intima–media thickness.[14] However, none of those trials determined ABI. The relation of EFT with CIMT may be explained by the effect of the pro-atherogenic and inflammatory mediators produced by the epicardial fat tissue and their influence in the progression of vascular damage.[5]

It is important to note that only one patient with an EFT <3 mm had a CIMT ≥0.9 mm, which is consistent with the association between visceral fat and atherosclerosis.

Aykan *et al*. found that EFT and ABI enabled the prediction of CAD severity in patients with suspected CAD and that combining ABI to EFT was additive for the prediction of CAD complexity, evaluated by the Syntax score.[15] However, they did not correlate ABI with EFT. Kim *et al*. found a significant correlation between EFT and arterial stiffness measured as brachial–ankle pulse wave velocity in patients with a normal ABI (>0.95),[16] whereas in our study, the patients had a lower ABI.

Our study has some limitations. Although echocardiography is non-invasive, less expensive and readily available than magnetic resonance imaging, it does not reflect total epicardial fat volume; hence, there are some concerns about its reproducibility.[16] Furthermore, we recognize that it is difficult to interpret the study findings in the absence of a control group.

Conclusion

We found that EFT correlates with CIMT in patients with metabolic syndrome, which reflects the association between visceral fat and atherosclerosis.

The measurement of EFT seems to be an independent predictor of atherosclerosis and should be measured as a part of the global cardiovascular risk evaluation in patients with metabolic syndrome.

Conflicts of interest. None declared

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