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Epicardial Adipose Tissue and Relationship with Coronary Artery Disease

Review Article

Alina Cristina Silaghi[1*], Raluca Pais[2], Ana Valea[1], Aurel Ion Mironiuc[3], Horatiu Silaghi[3]

[1] *Department of Endocrinology, County Clinic Emergency Hospital, Cluj-Napoca 400349, Romania*

[2] *2nd Department of Internal Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu", Cluj-Napoca 400006, Romania*

[3] *2nd Department of Surgery, University of Medicine and Pharmacy "Iuliu Hatieganu", Cluj-Napoca 400006, Romania*

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Abstract: Epicardial adipose tissue (EAT) is metabolically active tissue that accumulates around the coronary arteries. Epicardial fat is a rich source of free fatty acids and may contribute to local inflammatory load by increased synthesis of inflammatory cytokines. Direct passage of bioactive molecules into the coronary arteries due to close contact with the vascular wall and the lack of fascia may contribute to the pathogenesis of coronary artery disease. Direct correlation between visceral fat and EAT defines the latter as an indirect marker of intra-abdominal visceral adiposity. EAT is related to anthropometric and clinical features of the metabolic syndrome (MS) and to hepatic transaminases as markers of steatohepatitis. An increase in EAT thickness is related to an increase in left ventricular mass and is correlated with atrial enlargement and impairment in diastolic filling in obesity. Echocardiographic study of EAT is an easy and reliable imaging indicator of visceral adiposity and cardiovascular risk. EAT is an independent factor strongly correlated with significant coronary stenosis. A level of EAT above an established average value can be considered a predictive marker of cardiovascular risk. We review the most recent studies proving the specific active role of EAT in the development of cardiac disease.

Keywords: *Epicardial adipose tissue • Visceral adiposity • Cytokines • Coronary artery disease*

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1. Introduction

Obesity is a chronic and evolutionary disease related to the dysfunction of white adipose tissue. The increased prevalence of obesity, which has the potential of becoming a global epidemic, and its association with a high morbidity and mortality risk mainly due to cardiovascular causes have turned this condition into a public health priority. Anatomic distribution of the excessive adipose tissue plays an important role in the onset of metabolic complications, such as diabetes and dyslipidemia, as well as cardiovascular complications (e.g., hypertension and coronary disease).

Jean Vague was the first to indicate in 1947 the link between the severity of obesity due to the emergence of its complications and android or abdominal obesity [1]. This form of obesity is characterised by preferential accumulation of adipose tissue in the upper half of the body. Modern imaging techniques have led to improvement in the study of adipose tissue repartition and have indicated a preferential distribution of fat in the peritoneal cavity around abdominal viscera, allowing a much more accurate prediction of metabolic complications and cardiovascular risk [2].

A growing body of evidence shows that excessive development of other specific adipose depots such as cardiac, abdominal, or subcutaneous tissue or the

* *E-mail: alinasilaghi@yahoo.com*

accumulation of lipids outside the adipose tissue, such as in the liver or skeletal muscle, is also associated with metabolic and cardiovascular complications. This suggests that ectopic accumulation of lipids may influence the occurrence of obesity-related complications [3]. Ectopic depots of adipose tissue (e.g., epicardial and perirenal tissue) that have not been extensively studied thus far are relevant especially because of the local consequences of their excessive development.

In this article we review the most recent studies that have evaluated epicardial adipose tissue (EAT) in relation to visceral adiposity and have shown EAT's specific role as a cardiac risk marker and a potentially active player in the development of cardiac disease.

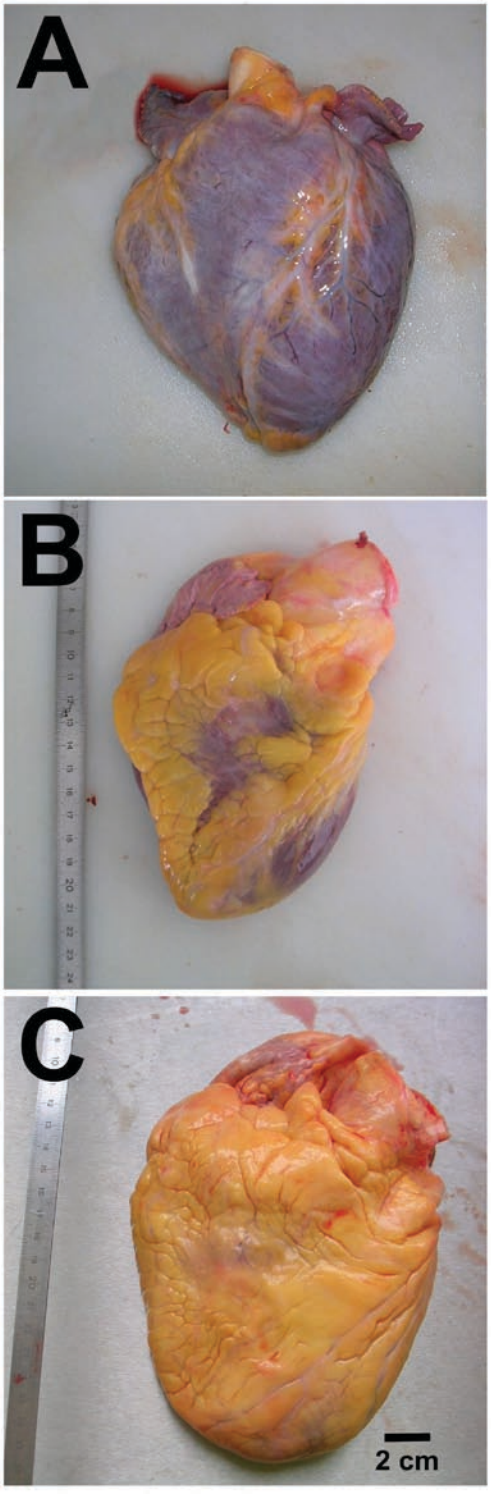
2. Anatomic features of epicardial adipose tissue

The study of human anatomy indicates that the surface of the heart is covered by a variable quantity of adipose tissue called pericardial adipose tissue. It consists of paracardiac and epicardial adipose tissue, the latter being situated between the visceral layer of the pericardium and the myocardium. Main coronary arteries, after their emergence from the aorta, are located on the surface of the myocardium in direct contact with and surrounded by EAT. The intramyocardial coronary course is exceptional; in almost all cases the main coronary arteries and their branches cross EAT before they reach the myocardium.

There is no evidence showing that this tissue provides mechanical protection for the heart. However, it has been noted that EAT might act as buffer tissue against torsion caused by arterial pulsatility and cardiac contraction and it might facilitate coronary arterial remodelling. EAT also represents a means for local storage of fat resulting from coronary circulation, regulating the homeostasis of free fatty acids (FFA) at this level. It is also a means for their release into the myocardium during energy-consuming activities [4]. According to a study on wild and domestic animals, EAT and the visceral abdominal adipose tissue (VAT) have common embryologic origins in brown adipose tissue [5].

In adults, EAT is mainly located in the anterior and posterior atrioventricular and interventricular sulci, extending from the base of the heart towards the apex (Figure 1). Small amounts of adipose tissue can also be found under the epicardium in the free wall of the atrial myocardium and around the atrial auricles. The larger the amount of epicardial adipose tissue, the more it fills the interventricular sulci, tending to cover the entire surface of the heart. The amount of EAT covering the

Figure 1. Images of excised hearts of human adults showing wide variability in the epicardial adipose tissue: (A) small quantity of EAT along the branches of the coronary arteries, (B) EAT depots extend over the anterior surface of the ventricles, (C) EAT massive depot including all the anterior surface of the heart. Bar = 2 cm.



right ventricle is three times higher than that covering the left ventricle. A small quantity of EAT follows the adventitia of coronary branches to their penetration in the cardiac muscle. All these indicate strong anatomic and functional connections between the myocardium and EAT. The two components of the heart, EAT and myocardium, share the same vascular support and are not separated from each other by fascia, as in the case of striated muscle [6].

A recent study has indicated that the African-American population has a smaller quantity of both adipose tissue (AT) and EAT compared to the white, non-Hispanic population, although the former have a higher risk for the development of obesity-related complications. This highlights the importance of the relationship between race and the distribution of AT [7].

3. Necropsy studies of the epicardial adipose tissue

In 1955 Reiner et al. [8] performed a descriptive necropsy study of EAT in hypertensive, ischemic, and normal patients in an effort to assess its importance in cardiac pathology.

Subsequently, Corradi et al. in another autopsy study that is considered more elaborate and more accurate investigated the relationship between EAT and ventricular myocardial mass in a series of 117 necropsies on adults [9]. The authors concluded that EAT and myocardial mass ratio is constant for each ventricle and it is not influenced by ischemia or myocardial hypertrophy. They showed that EAT and myocardial mass increase proportionally during the process of myocardial hypertrophy, suggesting that EAT is influenced by local factors, and not by the entire quantity of adipose tissue, as in obesity. Later, Iacobellis et al. [10] performed ultrasound studies on healthy subjects and showed that EAT is significantly linked with the mass of the left ventricle, regardless of age and body mass index (BMI). Our team's study [11], including 56 autopsies, also concluded that age, abdominal circumference, and the mass of the heart were the only variables independently correlated with EAT that represented independent predictive factors of EAT accumulation. EAT was not correlated with BMI or anthropometric measurements of the peripheral adipose tissue. The extension of EAT was associated with the severity of coronary artery disease in that it correlated with the degree of coronary stenosis.

4. Epicardial adipose tissue - source of inflammatory factors

4.1. Relationships between periadventitial inflammation and atherosclerosis

Atherosclerosis is the result of various mechanical, immunologic, and inflammatory factors acting at the level of the vascular wall. Recent in vitro studies have shown that inflammatory cytokines stimulate the proliferation of smooth muscle cells, indicating their role in atherosclerosis. At the same time, inflammatory changes at the level of the coronary arteries seem to have an important role in the occurrence of vasospasm and unstable angina. An increasing number of studies attest to changes at the adventitial level and suggest that even perivascular changes may alter vascular homeostasis. The theory of outside-to-inside cell passage has been elaborated by the occurrence of vascular intimal injury resulting from exposure to a number of factors of perivascular origin (e.g., extracoronary factors). In addition to intravascular factors, they could contribute to the occurrence of vascular lesions. The inflammatory mediators originating outside the coronary artery are capable of inducing compositional changes in the inner layer of the intima. In a study on pigs, the proximal segment of the coronary arteries was put in prolonged contact with IL-1β (interleukin-1β), a strong inflammatory cytokine involved in the pathogenesis of atherosclerosis. Those authors observed on the artery segments a thickening of the intima and induced histamine-based vasospasm. The severity of the lesions was clinically significantly decreased when anti-IL-1β antibody and platelet-derived growth factor (PDGF) were used in addition to IL-1β, highlighting the effect of this cytokine [12]. In another study on coronary arteries in pigs, the periadventitial application of monocyte chemoattractant protein (MCP)-1 and oxidized low-density lipoproteins (LDL) induced an accumulation of macrophages at the adventitial level. The activation of accumulated macrophages and release of inflammatory cytokines and endogenous chemokines favored the migration of the macrophages towards the intima. Long-term results included changes at the level of the intima, vascular geometric remodeling, and vasospasm. It was thus suggested that the bioactive molecules of the pericoronary tissue may alter arterial homeostasis [13]. Beneficial consequences of the local inflammatory reaction include the stimulation of the angiogenic response and the development of collateral circulation in patients with severe coronary artery disease.

4.2. Cytokines and the epicardial adipose tissue

The presence of metabolically active adipose tissue stored around the coronary arteries may contribute to the local inflammatory load. Direct passage of adipokines and FFA into the vascular wall due to the lack of fascia may thus lead to atherosclerosis and increased coronary risk. The coronary segments that are not surrounded by EAT or those with a partial intramyocardial path are protected from atherosclerosis. A study on rabbits fed a diet rich in cholesterol showed that segments with an intramuscular course were lesion-free [14,15], compared to those surrounded by EAT, a finding probably also due to the contribution of hemodynamic factors.

Perivascular adipose tissue synthesizes chemotactical factors such as IL-8 and MCP-1, and is responsible for leukocyte migration through the blood towards the area between the adventitia and the perivascular adipose tissue. Macrophages are more numerous and concentrated in the periadventitial fat of coronary arteries with a lipid core of atheromatous plaque compared with non-atherosclerotic or fibrocalcified coronary arteries [16].

In obese patients, EAT contains numerous pro-inflammatory adipokines and is infiltrated by macrophages, lymphocytes, and basophils [17]. Mazurek and collaborators [17] compared the expression of inflammatory factors in biopsy specimens of subcutaneous adipose tissue (SAT) and EAT in patients with severe coronary artery disease who did not have diabetes or obesity. The local expression of certain chemokines (MCP-1) and inflammatory cytokines (IL-1β, IL-6 and TNF-α) was higher in EAT than in SAT, showing that EAT may contribute to the coronary local inflammatory potential. The degree of local cytokine expression was disproportionate to their concentration in plasma. The authors also observed a higher infiltration of macrophages in EAT than in SAT.

Several mechanisms have been proposed to explain the inflammatory characteristics of EAT. The first hypothesis suggests that the effect of local ischemia-induced hypoxia leads to myocardial damage, as well as damage to adjacent EAT, with a consequent increase in redox status and increased expression of inflammatory cytokines. Another hypothesis considers the differentiation of preadipocytes from macrophages in obesity, with macrophages acknowledged as the most important source of cytokines [17].

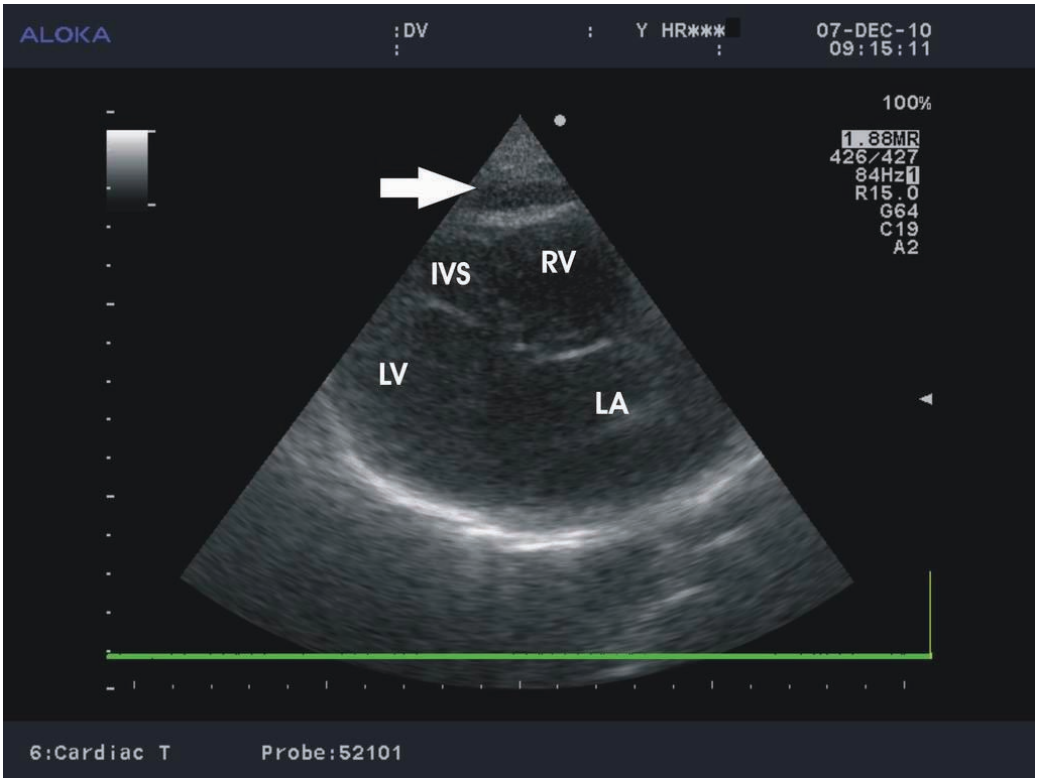
A recent study indicated that the release of inflammatory adipokines induced clinically significant changes in monocytes and coronary endothelial cells, with direct pathological implications for coronary atherosclerosis [18]. Iacobellis et al. [19] demonstrated for the first time that adiponectin, a vasoprotector anti-inflammatory adipokine, is expressed at the level of EAT. It is significantly lower in EAT in patients with coronary artery disease than in patients without that disease. Another recent discovery showed that the expression of the mRNAs coding for leptin and adiponectin are higher in SAT than in EAT. It is also higher in EAT in women than in men [20]. Increased levels of epicardial adiponectin are associated with the maintenance of sinus rhythm after cardiovascular surgery, which emphasizes the hypothesis of local inflammation in the pathogenesis of postoperative atrial fibrillation [21]. Resistin is an adipocitary factor correlated with insulin resistance; it has a higher expression in EAT, where it is secreted in levels comparable to VAT, than in the subcutaneous or gluteo-femoral tissues [22].

Visfatin is considered a marker of VAT, although, when compared to SAT, some studies have found no significant variation of visfatin mRNA expression in VAT [23]. Visfatin and plasminogen activator inhibitor-1 (PAI-1) have been found to have a higher plasma concentration in obese subjects than in non-obese subjects when these variables were correlated with the quantity of EAT and VAT measured by CT. The expression of omentin is higher in perivascular adipose depots and in EAT compared to in SAT [24].

Angiotensinogen mRNA expression is increased in EAT after cardiac surgery compared to the preoperative status, and it remains unchanged in SAT. Angiotensin converting enzyme and angiotensin receptor II type 1 mRNA expressions are comparable in EAT and SAT preoperatively and remain unchanged until completion of the surgery [25]. In recent years, a series of articles described a link between angiotensin II, oxidative stress, and insulin resistance [26,27], suggesting that an increase of angiotensinogen mRNA in EAT may contribute to insulin resistance observed in these patients after surgery.

Adrenomedulin (AM) is a cytokine that has significant vasodilatory and anti-oxidizing properties, and it is a potent angiogenic and anti-inflammatory molecule [28-30]. A study by our team has shown that mRNA expression of AM is significantly higher in EAT and SAT in patients with coronary artery disease compared to patients without the disease, suggesting a possible coronary protective role of adrenomedulin [31].

Figure 2. Transthoracic echocardiogram in the parasternal long axis view at the end of the systole, showing an echo-free area on the free wall of the right ventricle representing the epicardial fat. LA = left atrium; LV = left ventricle; IVS = interventricular septum; white arrow = epicardial adipose tissue.



5. Biochemical characteristics of EAT

The biochemical properties of EAT suggest its role as a metabolic and cardiovascular risk marker. It has been noted that EAT in laboratory guinea pigs releases a markedly higher quantity of FFA than visceral perirenal adipose tissue, indicating an increased lipolytic capacity [32]. This can be explained by two main mechanisms: the antilipolytic effect of insulin, which is lower in VAT, and the increased number of β adrenergic receptors at this level, especially β3, the stimulation of which activates lipolysis. It has been recently discovered that the fatty acid-binding protein 4 (FABP4/aP2) present in adipocytes and macrophages in atherosclerotic lesions is also expressed in EAT and is elevated in patients with metabolic syndrome [33].

Some features of EAT differentiate it from SAT: the small size of adipocytes; the content of certain fatty free acids and the high content of proteins; the high rate of incorporation of FFA in the EAT; the FFA synthesis, as well as the FFA degradation and insulin-sensitive lipogenesis; the low rate of glucose usage; and the low lipoprotein-lipase, stearol-CoA desaturase, and acetyl CoA alpha-carboxylase mRNA expression [33,34].

The increase of proteins involved in the oxidative stress in EAT compared to that in SAT in patients with coronary artery disease suggests an association with increased myocardial oxidative stress in this category of patients [35].

6. Clinical assessment of epicardial adipose tissue

6.1. Echocardiographic assessment of epicardial adipose tissue

Iacobellis et al. [10] were the first to perform and validate the measurement of EAT by two-dimensional and M-mode transthoracic echocardiography. Patients were placed in the left lateral decubitus position. The ultrasound examination required a recording of at least 10 cycles of two-dimensional long-axis and short-axis views of the heart and at least 10 cycles of M-mode with optimal cursor beam orientation in each view. For a correct assessment, the video recording had to be interpreted by two experienced sonographers. The coefficient of variation between the two different examiners was 3% in Iacobellis' study, indicating substantial reproducibility

of echocardiographic measurements. Epicardial fat thickness was assessed on the free wall of the right ventricle in two sections at the end of systole. EAT appeared as an echo-free space between the wall of the right ventricle and the pericardium. When the quantity of EAT was higher, it could even appear as hyperechoic [10].

There are two main reasons for measuring EAT in the free wall of the right ventricle at the end of the systole. First, this region is known to contain the thickest layer of EAT, and second, the parasternal ultrasound long-axis and short-axis views of the right ventricle allow for the most accurate measurement of EAT (Figure 2). If EAT is present, the hypertrophy of the trabecula of the right ventricle does not influence the assessment of EAT. These data suggest that echocardiographic assessment of EAT may be simple, risk-free, inexpensive, and accurate.

6.2. Relationships between epicardial adipose tissue measured by ultrasound and variables of the metabolic syndrome

A strong correlation has been demonstrated in both obese and non-obese patients between EAT thickness measured by ultrasound, waist circumference, and VAT as assessed by magnetic resonance imaging (MRI) or computerized tomography (CT) [36-39]. EAT does not correlate with BMI, since it is not linked with either overall weight increase or SAT. It is known that VAT is correlated with metabolic and cardiovascular risks in obesity. Thus, ultrasound measurement of EAT might be successfully used in VAT evaluation in both clinical practice and research [40].

The same authors indicated that ultrasound-measured EAT correlates with the main clinical and anthropometric variables of the metabolic syndrome (MS): circumference of the waist, fasting insulinemia, diastolic hypertension, LDL-cholesterol, plasma adiponectin, HDL-cholesterol, and systolic hypertension [38], as well as with age, C reactive protein (CRP) and Homeostatic Model Assessment score [41]. Clinically significant weight loss resulting from adherence to a hypocaloric diet [42] or bariatric surgery [43] leads to a marked decrease of both VAT and EAT. This is accompanied by improvement not only of the variables of the metabolic syndrome but also of morphologic and functional characteristics of the heart. The quick and easy ultrasound assessment of EAT might be used both to indirectly assess and monitor the thickness of VAT after bariatric surgery [44] and to assess certain medications that induce weight loss or act on AT, such as thiazolidindiones, fibrates, angiotensin receptor blockers, highly active antiretroviral therapy, and hormonal therapy.

6.3. Assessment of epicardial adipose tissue by CT and MRI

Measurement of EAT thickness by CT uses the same guidelines as those outlined in ultrasound assessment. For the appropriate study of the four chambers of the heart, the sections should be oblique and axial, with a thickness of 10 mm [45]. A study with CT showed that volumetric measurement of EAT had a reproducibility (coefficient of variation between 3-5%) superior to simple measurements such as linear or EAT area (coefficient of variability 11 -23%), and it positively correlated with markers of obesity and metabolic syndrome [46]. EAT volume measured by CT is associated with obesity, coronary-artery calcification score, metabolic syndrome, and coronary artery disease. This noninvasive method can be successfully used along with coronary angiography and coronary calcification score to detect and assess coronary risk.

Some observers have shown that volumetric EAT measurement by CT and MRI is more accurate and its reproducibility is superior to linear measurements [47,48] and correlates more accurately with the extension of coronary lesions [49,50]. To obtain EAT mass, some authors have suggested manual delineation of EAT area on MRI. The value of EAT area was multiplied by section thickness and then converted to grams by the specific AT density of 0.9196 g per milliliter [51].

7. Relationships between epicardial adipose tissue and functional characteristics of the heart

Obesity is associated with morphologic changes of heart, especially the left ventricle (LV), the pathophysiologic mechanism of which is not fully understood. Although some studies have reported a positive correlation between BMI and increased LV mass [52-55], others have found no relation [56-60]. In subjects with uncomplicated obesity [57], no link was found between increased weight and LV mass, LV geometry changes, or ventricular hypertrophy, when the values were comparable to subjects of normal weight.

Pericardiac AT could have a role in the occurrence of cardiac morphologic changes. The studies seem to point to EAT, which could have a functional or mechanical association, as a contributor to the LV morphological abnormalities in obesity. EAT measured by ultrasound

correlates with LV mass, as shown in the study with ultrasound on obese subjects by Iacobellis [61], and as it was previously demonstrated in Corradi's necropsy study.

LV mass is calculated by applying Devereux's anatomic formula. This correlation is independent of age and BMI, which reflects total adiposity, contrary to other results reported in a previous study [62]. EAT is not correlated with LV-wall thickness, suggesting that other major factors act on ventricular geometry, such as hypertension or coronary heart disease. An increase in visceral fat appears to have a direct effect on LV ejection fraction, cardiac output, and perfusion of the entire body. At the same time, the biochemical properties of visceral fat such as insulin resistance, high levels of FFA, and increased beta-adrenergic activity may contribute to LV hypertrophy.

A strong link between obesity and diastolic dysfunction, evidenced by altered LV relaxation time or an increase in myocardial-wall resistance, gradually leads to increased force of atrial contraction and dilatation. This has also been described in uncomplicated obesity [58-60].

A relationship between diastolic dysfunction, hyperinsulinism, and hyperglycemia has been suggested, whereby insulin resistance (IR) affects the biochemical mechanisms of diastolic relaxation time, affecting actin-myosin coupling due to lack of calcium uptake in endoplasmic reticulum [63].

Recently, Iacobellis et al. [64] assessed the relationship between EAT, which is considered by the same authors as a new marker of visceral adiposity, atrial dimensions, and diastolic function. It has been shown that an increase in EAT is significantly correlated with altered diastolic filling characteristics and with increased bilateral atrial dimensions in subjects with morbid obesity. This correlation was independent of BMI, age, and sex. An increase in EAT may have a mechanical effect on the diastolic filling of both the left and right ventricles, with subsequent atrial dilatation, which are potential risk factors for the development of atrial fibrillation in obese subjects. In massive obesity, there is probably a concomitant increase in EAT, BMI, and insulin resistance that leads to impaired diastolic filling and atrial dilatation. More recent studies confirm previous observations supporting an association between EAT, glucose levels, and diastolic function in patients with diabetes [65].

8. Relationships between EAT and non-alcoholic fatty liver disease

In patients with increased VAT who have high levels of metabolic and cardiovascular risk, Iacobellis et al. [66] demonstrated a positive correlation between EAT and hepatic transaminases as markers of non-alcoholic fatty liver disease (NAFLD). This correlation was independent of BMI.

Another study assessed the relationship between EAT, NAFLD, and IR in obese patients and showed that EAT is a more sensitive variable than steatosis in assessing the risk of obesity complications [67]. EAT measured by ultrasonography was correlated with the degree of ultrasound-assessed steatosis and with abdominal AT evaluated by dual energy x-ray absorptiometry (DEXA), as well as with MS characteristics [68].

In another study [69], in young non-diabetic patients with hepatic steatosis, the surface of the intrapericardial and extrapericardial AT was higher than in those without steatosis, when assessed by hepatic and cardiac spectroscopic MRI, respectively. There were no detectable changes in LV morphologic features or systolic and diastolic function in subjects with hepatic steatosis. However, an abnormality of LV metabolism was detected, as assessed by a very low phosphocreatine/adenosine triphosphate ratio [69].

9. Epicardial adipose tissue and cardiovascular risk

A survey of women in menopause [46] showed that EAT thickness measured by CT at the level of the main coronary arteries was positively correlated with cardiovascular risk factors like age, weight, waist circumference, smoking, glycemia, and systolic blood pressure. A negative correlation was established between EAT and HDL-cholesterol, as well as a correlation between EAT and the degree of coronary calcification on CT. These correlations between EAT, cardiovascular risk factors, and coronary calcification support the hypothesis that EAT could be related to coronary atherosclerosis.

Three-dimensional intravascular ultrasound reconstruction images have shown that coronary atherosclerotic plaques are predominantly eccentric, are accompanied by positive remodelling of the vascular wall, and present with a pericardial distribution (a myocardial distribution is rare or absent), possibly in connection with an external factor that could be EAT [70]. Using ultrasound measurements of EAT and coronary

angiography assessment for the degree of coronary stenosis, Ahn et al. [41] reported that EAT is significantly thicker in patients with coronary artery disease than in healthy subjects, and it correlates with insulin resistance and inflammatory markers [41,71]. The EAT layer is significantly thicker in patients with unstable angina compared to those with stable angina or atypical chest pain.

EAT is one of the independent factors that can induce a clinically significant coronary stenosis, along with smoking, age, and diabetes mellitus [72]. Most studies have found a correlation between EAT (measured by ultrasonography) and the existence of coronary artery disease (assessed by coronarography) or its severity [73-75].

In a recent study, Iacobellis et al. [76] established average values above which EAT can be considered a predictive marker of cardiovascular risk. They are 9.5 mm for men and 7.5 mm for women.

It is known that HIV-positive patients present with accelerated atherosclerosis and increased cardiovascular risk. Treatment with recently introduced highly active antiretroviral medication is correlated with metabolic syndrome and lipodystrophy (LDS) and with increased VAT and decreased SAT mass. In these patients, ultrasound assessment of EAT is correlated with ultrasound measurement of intima-media thickness at the carotid level [77] and VAT (assessed by MRI). Thus, EAT has been shown to be a reliable marker of visceral adiposity and an index of subclinical atherosclerosis in patients with HIV and metabolic syndrome with LDS [78].

In patients with growth hormone deficiency with or without replacement treatment, a higher quantity of EAT has been detected after ultrasound measurement. EAT can be correlated with VAT and then used as an indicator of long-term cardiovascular risk in this population [79].

10. Conclusions

EAT is considered to be metabolically active tissue that accumulates around the coronary arteries and may contribute to local inflammatory load by increased synthesis of pro-inflammatory adipokines and homeostasis proteins. Direct passage of adipokines and FFA from EAT towards the coronary arteries and myocardium due to direct contact with the vascular wall and the lack of fascia may lead to atherosclerosis and increased coronary risk. Direct correlation of VAT to EAT defines the latter as indirect marker of intra-abdominal visceral adiposity. EAT assessment by ultrasound is a simple, noninvasive, accurate and reproducible method that can be used in clinical practice to evalute cardiovascular risk. All these findings suggest that the decrease of the inflammatory status of EAT is a new therapeutic target in the primary prevention of coronary atherosclerosis and leaves room for future studies on this tissue.

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