Clinical importance of epicardial adipose tissue

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Abstract

Different visceral fat compartments have several systemic effects and may play a role in the development of both insulin resistance and cardiovascular diseases. In the last couple of years special attention has been paid to the epicardial adipose tissue (EAT), which can be quantified by non-invasive cardiac imaging techniques. The epicardial fat is a unique fat compartment between the myocardium and the visceral pericardium sharing a common embryologic origin with the visceral fat depot. Epicardial adipose tissue has several specific roles, and its local effects on cardiac function are incorporated in the complex pathomechanism of coronary artery disease. Importantly, EAT may produce several adipocytokines and chemokines that may influence – through paracrine and vasocrine effects – the development and progression of coronary atherosclerosis. Epicardial adipose tissue volume has a relatively strong genetic dependence, similarly to other visceral fat depots. In this article, the anatomical and physiological as well as pathophysiological characteristics of the epicardial fat compartment are reviewed.

Key words: coronary artery disease, epicardial adipose tissue, insulin resistance syndrome, visceral fat compartments, epicardial fat.

Introduction

Type 2 diabetes mellitus due to its prevalence rate and cardiovascular complications carries a serious burden for health care systems worldwide [1]. Insulin resistance syndrome with the dysfunction of the abdominal fat compartment plays an important role in the disease development [2, 3]. In the last couple of years it was documented that other fat compartments may also be involved in the insulin resistance syndrome and may contribute to the pathogenesis of atherosclerosis [4]. Recently, special attention has been paid to the epicardial fat compartment [5].

In the 19th century it was believed that fatty degeneration of the heart is the main cause of every heart disease [6]. Richard Quain was the most well-known proponent of this theory, recognizing the relationship of increased fat volume on the epicardial surface with coronary artery obstruction. The diagnosis of fatty heart was very popular in the Victorian era but was later changed to fibrosus heart disease and chronic myocarditis. All these diagnoses were replaced by the ischemia theory in the middle of the 20th century. Interestingly, it was recognized at that time that 70% of the fatty heart diagnoses in Quain's pathological records corresponded with ischemic heart disease. Although the relationship between increased epicardial fat and cardiac diseases was described nearly 150 years ago, medicine did not dedicate too much attention to this

field. However, cardiovascular research has begun to explore the role of different fat compartments in line with the pandemic spread of obesity and the dynamic development of radiological imaging techniques [7]. In this regard, special attention was paid to the epicardial fat due to its anatomical proximity with the coronary arteries [8]. While anatomical and biochemical characteristics of the epicardial fat compartment were described in early studies, its potential role in the pathomechanism of coronary artery disease (CAD) and other cardiac dysfunctions has only been investigated recently.

In this article, the anatomical and physiological as well as pathophysiological characteristics of the epicardial fat compartment are reviewed.

Terminology

The terminology of fat compartments around the heart is not standardized; there are still many imprecise uses of these definitions in the literature. Nevertheless, the most widely used and accepted terms are summarized in Table I.

The epicardial fat as a part of the visceral fat is localized between the myocardial surface and the visceral layer of the pericardium. Pericardial fat involves adipose tissues between the two (visceral and parietal) pericardial layers and the fat depot on the external surface of the parietal pericardium. Paracardial fat contains fat deposits outside the parietal pericardium and therefore sometimes is called extra-pericardial intrathoracic fat. The coronary arteries are surrounded by the perivascular/pericoronary fat, irrespective of location. The term ectopic fat implies triglyceride deposits in non-adipose tissue of different organs such as myocardium, liver, pancreas, etc. [9].

The clear distinction of epicardial fat from pericardial fat is of great clinical importance [10]. In the embryological aspect they differ from each other. While the epicardial fat is similar to the visceral fat and originates from mesodermal cells, the pericardial fat has an ectodermal origin, similar to subcutaneous fat. Moreover, there is also a difference in the blood supply between these two fat compartments; the epicardial fat is supplied by the small myocardial coronary arteries, while the circulation of pericardial fat is provided from the thoracic vessels. The amount of epicardial and pericardial fat compartments as a percentage of total cardiac mass also differs (Table II).

Cardiac imaging of epicardial adipose tissue

Epicardial fat tissue can be visualized and quantified non-invasively by echocardiography, magnetic resonance imaging (MRI) and cardiac computed tomography (CT).

Echocardiography provides a simple, cheap and readily available assessment which directly pictures the epicardial adipose tissue (EAT) thickness on the free wall of the right ventricle. Imaging by echocardiography provides the parasternal short- and long-axis view in three consecutive end-systolic phases (Figure 1). Several studies have estab-

Table I. Terminology of fat compartments around the heart

Visceral fat	Adipose tissue around the visceral organs
Epicardial fat	Visceral fat between the myocardial surface and the visceral layer of the pericardium
Pericardial fat	Adipose tissue between the two pericardial layers (visceral and parietal pericardium) and fat depot on the external surface of the parietal pericardium
Paracardial fat	Fat deposits outside the parietal pericardium (extra-pericardial thoracic fat)
Perivascular (pericoronary) fat	Adipose tissue around the vessels (coronary arteries) irrespective of location
Ectopic fat	Lipid (triglycerides) deposits in non-adipose tissue (i.e. myocardium, liver, pancreas, etc.)

Table II. Differences between epicardial and pericardial fat compartments

Variable	Epicardial fat	Pericardial fat
Location	Between the myocardial surface and the visceral pericardium	Outside the visceral pericardium, between the visceral and parietal pericardium and on the external surface of the parietal pericardium
Embryologic origin	Splanchnopleuric mesoderm	Primitive thoracic mesenchyme
Blood supply	Branches from the coronary arteries	Non-coronary sources (branches from the internal mammary artery)
Amount	20% of total heart weight	20–40% of cardiac mass

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Figure 1. Quantification of epicardial adipose tissue by echocardiography (parasternal view). The thickness of the area between the myocardium and the visceral layer of the pericardium is 0.85 cm, indicating epicardial adipose tissue
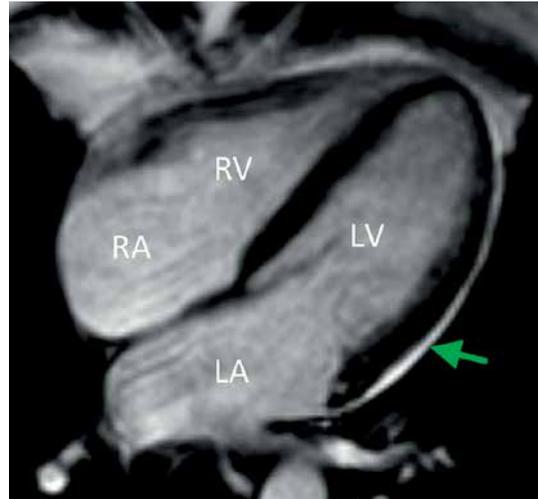

Figure 2. Epicardial adipose tissue (arrow) by using magnetic resonance imaging (MRI) technique

RA – right atrium, LA – left atrium, RV – right ventricle, LV – left ventricle.

lished the general EAT thickness under 7 mm in the asymptomatic population [11]. Nevertheless, this method has several disadvantages including poor reproducibility and high dependence on the observer's experience. In addition, it may not reflect accurately the whole quantity of the epicardial fat due to the two-dimensional nature of the measurement. In other words, the thickness rather than the entire quantity of the pericardial fat compartment can be assessed by echocardiography. Moreover, the method has poor intra- and interobserver variability, and its results may differ significantly from the measurements with CT [12].

In contrast to echocardiography, MRI provides accurate area measurements with enhanced spin-echo sequence and, in this way, EAT area mass and volume can be calculated (Figure 2). Area measurements with MRI correspond well with fat thickness determination with echocardiography, although the Bland-Altman analysis shows a systemic bias through overestimation of EAT with echocardiography [13]. Magnetic resonance imaging is hardly available in routine clinical practice, is more expensive and has poorer spatial resolution compared to CT.

True volume assessment of EAT is feasible using cardiac CT. The three dimensional (3D) image reconstruction with multidetector-row CT (MDCT) has the best spatial resolution among the imaging modalities (Figure 3). It is of note that the specificity and sensitivity of measurements with MDCT are the best when compared to alternative imaging methods. The epicardial fat quantification is performed on prospectively ECG triggered non-contrast CT scans which extend from the pulmonary artery bifurcation to the diaphragm. The identification of the EAT is based on thresholds of CT attenuation. Typically, lower thresholds of CT attenuation range from –250 to –190 Hounsfield units (HU), and upper thresholds are
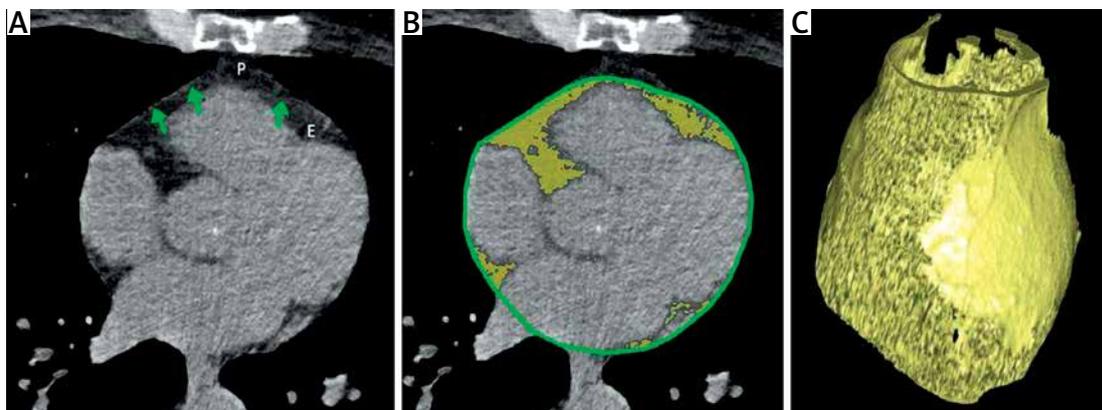

Figure 3. Measuring epicardial adipose tissue by cardiac computed tomography (CT). **A** – Axial section at the aortic root. Arrows indicate the visceral layer of the pericardium. Epicardial fat (E) is located inside and pericardial fat (P) outside the visceral layer. **B** – The visceral layer of the pericardium is traced manually (green). Epicardial adipose tissue (yellow) is marked automatically at the corresponding section. **C** – Three-dimensional reconstruction of the total epicardial fat compartment (yellow). The volume of epicardial adipose tissue was 112 cm^3

set between −50 and −30 HU. In contrast to area and thickness measurements, volume quantification provides the most accurate way for assessing the true epicardial fat quantity [14]. Using this method, coronary artery calcification may also be quantified, resulting in more reliable cardiovascular risk assessment [15]. Importantly, native CT results in a very small (1 mSv) radiation dose. Maurovich-Horvat *et al.* found in a collaborative study that the measurement of pericoronary adipose tissue was highly reproducible when using MDCT [16].

Anatomical characteristics of epicardial adipose tissue

In physiological circumstances the epicardial fat covers nearly 80% of the heart surface. According to previous observations this fat compartment contributes 20% to the whole heart quantity [17]. The EAT-covered heart region includes the heart base and the apex, the atrioventricular sulci, the entire surface of the right ventricle, and the great coronary vessels with their origins. The distribution of EAT is mostly inhomogeneous; the biggest mass is localized on the lateral and anterior walls of the right atrium, but in normal circumstances it also covers the atrioventricular and the interventricular sulci and the main coronary arteries as well. In the case of extremely enlarged EAT, it can also accumulate on the surface of the left atrium and along the vessel's adventitia with spreading into the myocardium. It is of note that there is no separating fascia layer between the epicardial fat and the myocardium, providing close proximity of these two different tissues [18]. In histological investigations it has been previously established that adipocytes in the EAT are smaller than those in the abdominal or the subcutaneous fat compartments [19]. Besides adipocytes, EAT includes nerves, ganglions, vessels, inflammatory cells and fibrocytes as well (Figure 4).

Age, gender, body weight and ethnicity should be taken into consideration among physiological determinants of EAT. Epicardial adipose tissue seems to increase with age [20]. The quantity of EAT depends on gender and body mass index (BMI). For example, pericardial fat was reported to be 137 ±54 cm^3 among men and 108 ±41 cm^3 among women of the Framingham offspring cohort [21]. In patients with a high BMI (> 27 kg/m^2), EAT volume was more than two times higher compared to those with a BMI < 27 kg/m^2 (155 ±15 cm^3 vs. 67 ±12 cm^3) [22]. Some ethnic differences in epicardial and pericardial fat thickness may also occur; non-Hispanic White men have more epicardial and pericardial fat than do African Americans [23].

The biochemical features of small adipocytes in EAT may also differ from those of other fat compartments. In experimental studies EAT had a higher rate of free fatty acid (FFA) release than adipose tissue elsewhere in the body, suggesting that EAT might play a role in local energy supply for the myocardium. In addition, a lower oxidative capacity and a lower rate of glucose utilization were also documented [24]. On the other hand, a 5-fold higher expression of uncoupled protein-1 (UCP-1) was found in EAT compared to other fat depots [25]. Uncoupled protein-1 is a specific protein in brown fat which is necessary for its energy production, and does not appear in other types of fat tissues. This latter feature is in line with the fact that epicardial fat evolves from brown adipose tissue during embryogenesis.

Physiological function of epicardial adipose tissue

Several physiological functions of EAT are already known from different studies or inferred from its biochemical or anatomical features. Unfortunately, experimental evidence supporting these observations are limited due to the very small amount of EAT in experimental animals (rodents).

It is suggested that functions of EAT may include protection of the myocardium against hypothermia [25]. In addition, EAT can provide a mechanical protective role for coronary circulation. It can attenuate the torsion developed by the myocardium contraction or the arterial pulse wave, but it has a permissive role as well in positive remodeling of coronary arteries [26].
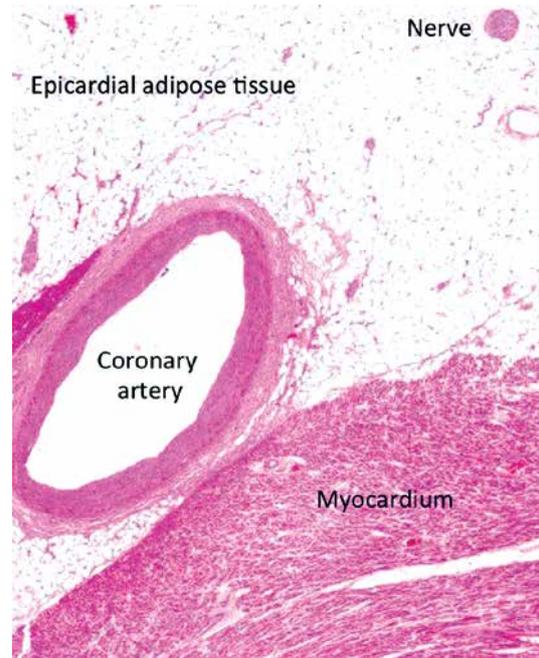

Figure 4. Microscopic view of the epicardial adipose tissue. It is of note that there is no separating fascia layer between the epicardial fat and the myocardium

Also, EAT has a substantial role in energy supply to the myocardium and should be considered as a provider of energy during periods of high energy demand [27]. On the other hand, EAT may protect the myocardium from the cardiotoxic effect of a large amount of FFA due to its capacity for fast FFA utilization [28]. Taken together, EAT may serve as a unique energy buffering pool in the homeostasis of the myocardium.

In addition, adiponectin secretion from epicardial adipocytes may promote the coronary circulation. Adiponectin improves endothelial function through stimulation of nitrogen monoxide synthase, reduces oxidative stress, and indirectly decreases the level of interleukin-6 (IL-6) and C-reactive protein (CRP) by reducing tumor necrosis factor-α (TNF-α) production [29, 30]. Adiponectin also has some extracardial effects such as increased glucose utilization in the hepatocytes and muscle cells which may result in improving insulin sensitivity [31].

Epicardial adipose tissue in the pathomechanism of atherosclerosis

Some years ago a hypothesis about the direct role of EAT in the development and progression of coronary atherosclerosis was raised, and paracrine and vasocrine effects of EAT due to close proximity of epicardial fat to coronary arteries were posited [32]. The hypothesis was indirectly supported by a pathological study in subjects with a myocardial bridge. Namely, no atherosclerosis was observed in coronary segments at the myocardial bridge where surrounding fat on the coronary arteries was lacking [33].

In a landmark study, Mazurek *et al.* analyzed epicardial and subcutaneous fat from the lower extremity in obese patients referred for coronary artery bypass grafting. They found increased levels of inflammatory mediators (IL-6, TNF-α, interleukin-1β (IL-1β), monocyte chemoattractant protein-1 (MCP-1)), macrophages, lymphocytes and basophils in epicardial fat as compared to subcutaneous fat compartments [34]. Others found that epicardial and omental fat exhibited a broadly comparable pathogenic messenger ribonucleotide acid (mRNA) profile indicating macrophage infiltration into the epicardial fat [35]. In another study, mediators of the nuclear factor-κB (NF-κB) and c-Jun N-terminal kinase (JNK) pathways were suggested to be involved in the inflammatory profile of EAT, highlighting the role of the macrophages in the inflammation within this tissue [36]. These studies indicate that chronic inflammation occurs locally as well as systemically, potentially contributing further to the pathogenesis of CAD.

It was documented that the epicardial adipocytes had impaired adiponectin secretion and increased leptin production in obese patients with hypertension, metabolic syndrome and CAD [37, 38]. This shift in the adiponectin/leptin ratio enhances the development of atherosclerosis. Namely, the decreased adiponectin expression attenuates endothelial function and leads to increased TNF-α production, triggering systematic inflammation and oxidative stress. The altered leptin level promotes atherogenic changes in endothelial cells such as increased adhesion of monocytes, a higher level of macrophage-to-foam cell transformation, unfavorable changes in lipid levels, and elevation of CRP and inflammatory cytokine levels. All these alterations may lead to development and destabilization of atherosclerotic plaques in coronary arteries [5].

Based on several studies it became widely accepted that EAT should be considered as a source of inflammatory mediators that might directly influence the myocardium and coronary arteries (Figure 5). Two mechanisms of influence (paracrine
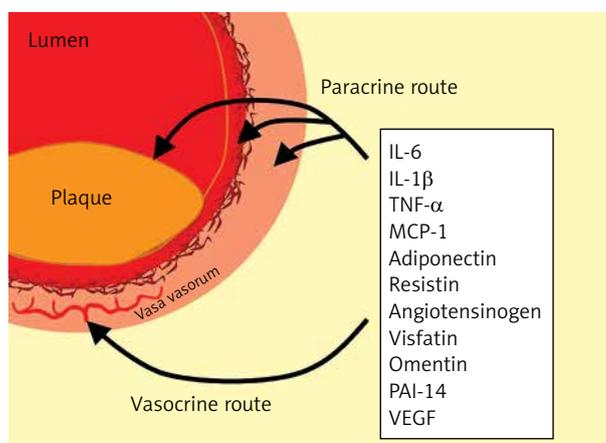

Figure 5. Routes for paracrine and vasocrine effects of epicardial adipose tissue on coronary arteries and plaque formation

IL – interleukin, TNF-α – tumor necrosis factor-α, MCP-1 – monocyte chemoattractant protein-1, PAI-1 – plasminogen activator inhibitor-1, VEGF – vascular endothelial growth factor.

and vasocrine) were suggested [39]. The paracrine way of influence means that adipokines released from pericoronary fat may diffuse across the arterial wall (adventitia, media, and intima) and finally can interact with endothelial cells in the intima and with vascular smooth cells in the media. The alternative vasocrine way of effect can be achieved by release of adipocytokines and FFAs from EAT directly into the vasa vasorum of the coronary arterial wall [40]. It was suggested that the vasocrine way of influence may be predominant over the paracrine effect in the case of more advanced atherosclerotic lesions where inflammatory mediators may diffuse only with difficulties [35].

The association between EAT thickness and the metabolic syndrome was documented in a recent meta-analysis [41]. The relationship of EAT with CAD has been analyzed by several clinical studies [42, 43]. In the Framingham and the MESA (Multiethnic Study of Atherosclerosis) epidemiological studies a significant association of epicardial fat with coronary artery calcification was found, which remained significant after adjustment for traditional cardiovascular risk factors [44, 45]. The increased epicardial fat proved to be associated with more advanced atherosclerosis in another study [46]. Epicardial fat was associated with non-calcified coronary plaques as well [47, 48]. A significant relationship of increased epicardial fat volume (> 130.7 cm^3) with vulnerable plaques was also documented [49]. The relationship of morphological features of vulnerable plaques (positive remodeling, spotty calcifications, and low CT attenuation in the necrotic core) to the pericardial fat was also studied, and the volume of pericardial fat proved to be nearly twice as high in patients with vulnerable plaques as compared to those without CAD [50]. Pericardial fat was associated with myocardial ischemia detected by single photon emission computed tomography (SPECT) in patients without known CAD [51]. Epicardial adipose tissue correlated with the degree of coronary atheromatosis, suggesting that its excessive accumulation might contribute to the development of acute coronary syndrome and coronary total occlusions [52]. In another study, EAT thickness was independently associated with the Thrombolysis in Myocardial Infarction (TIMI) risk score in patients with non-ST-elevation myocardial infarction (NSTEMI) and unstable angina pectoris [53]. In patients with the metabolic syndrome, increased EAT was associated with impaired coronary flow reserve [54]. In a different patient population (in women with chest pain and angiographically normal coronary arteries), EAT thickness was correlated with reduced coronary flow reserve [55]. Different surrogate parameters of atherosclerosis were also investigated by others, and an

association between EAT thickness and carotid intima-media thickness in type 2 diabetic patients as well as in children and adolescents with obesity was found [56, 57]. Moreover, EAT showed an independent association with arterial stiffness in an asymptomatic Korean cohort [58]. In a recent study, Maurovich-Horvat et al. investigated the relationship of different thoracic fat depots with coronary atherosclerosis and found an independent association between pericoronary fat and CAD. In addition, pericoronary fat correlated with inflammatory biomarkers as well, suggesting that while systemic inflammation plays a role in the pathogenesis of CAD, additional local effects may exist [59]. In a systematic review and meta-analysis, an association between the elevated location-specific thickness of EAT at the left atrioventricular groove and obstructive CAD was found [60].

Epicardial adipose tissue and other cardiac abnormalities

The relationship of EAT with atrial fibrillation was analyzed in several clinical studies. A strong association between EAT and atrial fibrillation (both paroxysmal and persistent) was documented by Al Chekakie et al.; the relationship proved to be independent of traditional risk factors and atrial enlargement [61]. In another study, EAT thickness was verified as an independent predictor for post-ablative recurrence of atrial fibrillation [62]. In patients with peritoneal dialysis, increased EAT was associated with impaired left ventricle diastolic capacity independently of CRP level, a marker of systemic inflammation [63].

Epicardial adipose tissue necrosis: a benign cause of chest pain

Epicardial fat necrosis is a rare clinical condition; 26 cases were reported up to 2011 [64]. It should be considered in the differential diagnosis of chest pain. The etiology is obscure, but the prognosis is good. In general, the presenting symptom is left-sided chest pain in a previously healthy individual with an associated juxtacardiac mass seen in chest radiography. The CT or MRI may confirm the correct diagnosis, resulting in the avoidance of surgical intervention.

Epicardial adipose tissue in type 2 diabetes, obesity and the insulin resistance syndrome (metabolic syndrome)

Typically, type 2 diabetes is preceded by prediabetes, but insulin resistance syndrome due to obesity may be the first pathological stage in the long-lasting asymptomatic period of diabetes. The insulin resistance syndrome (also called the metabolic syndrome) includes insulin resistance and

different metabolic abnormalities (elevated serum triglycerides, lower HDL cholesterol, hyperglycemia) as well as elevated blood pressure. Obesity, especially abdominal visceral fat accumulation, plays a central role in this syndrome. Although the use of the term and the suggested pathomechanism of the metabolic syndrome became debatable some years ago, the association between an enlarged abdominal visceral fat compartment and increased cardiovascular risk remained unquestionable [65]. The enlarged visceral fat depot is characterized primarily by increased lipolysis leading to hepatic steatosis. Non-alcoholic fatty liver disease (NAFLD) is often regarded as the hepatic manifestation of insulin resistance [66] and is considered as a novel predictor of cardiovascular disease [67, 68].

Several clinical investigations have aimed to assess the characteristics of EAT in the metabolic syndrome, prediabetes and type 2 diabetes. In a meta-analysis, EAT was 7.5 ±0.1 mm in thickness in the metabolic syndrome ($n = 427$) compared to 4.0 ±0.1 mm in controls ($n = 301$), and EAT correlated significantly with the components of the metabolic syndrome [69]. Epicardial adipose tissue volume was significantly higher in patients with type 2 diabetes than in nondiabetic subjects, and EAT volume was significantly associated with components of the metabolic syndrome [46]. In asymptomatic type 2 diabetic patients the thickness of EAT proved to be an independent risk factor for significant coronary artery stenosis but not for silent myocardial ischemia [70]. A strong correlation was found between fasting plasma glucose and EAT measured with CT or echocardiography [71, 72]. Epicardial adipose tissue quantity was higher in patients with type 2 diabetes mellitus compared to lean subjects or obese patients without diabetes. In addition, the difference in EAT volume between men and women was more pronounced in subjects with impaired fasting glucose or diabetes mellitus [73]. A clear relationship of epicardial fat and serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activity, surrogate markers of fatty liver, was documented in a cross-sectional, observational study [74]. Taken together, the insulin resistance syndrome (the metabolic syndrome), type 2 diabetes, NAFLD and CAD are associated with an increased amount of epicardial fat [75].

In the majority of studies an increase of EAT volume was associated with stenosis of the coronary arteries [76, 77]. Since these studies are cross-sectional, it is uncertain whether adipose tissue plays a causal role in the development of atherosclerosis. Importantly, two longitudinal studies have reported results that support the hypothesis of 'outside to inside signaling' as a cause

of atherosclerosis [45, 78]. In these studies, intrathoracic and EAT volume were measured and an increase of the quantity of intrathoracic and EAT was associated with incident coronary heart disease and with major adverse cardiac events. Associations were independent from BMI and other risk factors, suggesting that EAT is one of the factors contributing to CAD.

Epicardial adipose tissue in type 1 diabetes

Interestingly, higher epicardial fat and serum leptin levels were found in subjects with type 1 diabetes than in non-diabetic controls. The epicardial fat thickness and serum leptin levels proved to be the best independent correlates of each other in patients with type 1 diabetes independently of BMI, glycemic control and daily insulin requirement [79]. Recently, patients with type 1 diabetes ($n = 100$) from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study were investigated. In this pilot study, the accumulation of adipose tissue in epicardial and intra-thoracic spaces was strongly associated with higher BMI, greater waist-to-hip ratio, higher weighted glycated hemoglobin values, elevated triglycerides and a history of elevated albumin excretion rate or end-stage renal disease [80].

Role of genetic effects on epicardial adipose tissue

As EAT and other abdominal fat compartments (subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), hepatic lipid accumulation) carry different clinical significance [81] and epicardial fat differs from pericardial fat from an embryological point of view, the role of genetic effects on EAT and other fat compartments may differ. In a classical twin study with CT investigation our preliminary results indicated that EAT had a relatively strong genetic dependence, similarly to BMI and waist circumference [82, 83]. In contrast to abdominal fat compartment areas, a weak genetic and a stronger environmental dependence of hepatic lipid accumulation was found in our twin cohort [84].

Treatment options for modifying epicardial adipose tissue volume

Lifestyle changes, bariatric surgery and various drugs may be applied. Reduction in weight (BMI) by using a very-low calorie diet or exercise training program in obese patients is associated with a decrease in EAT volume [85, 86]. Nevertheless, this was observed after bariatric surgery as well, although myocardial triglyceride content did not change significantly [87]. In a meta-analysis, diet

or bariatric surgery proved to be more beneficial than exercise training in reducing EAT volume [88]. The effect of drugs on EAT is controversial. Atorvastatin resulted in a more pronounced decrease of EAT than simvastatin/ezetimibe [89]. Pioglitazone compared with metformin increased pericardial fat volume in patients with type 2 diabetes [90]. Short-term (3 months) use of glucagon-like-receptor agonists (exenatide, liraglutide) decreased the volume of EAT in type 2 diabetic patients [91]. In a longer (26 weeks) randomized controlled trial, exenatide twice daily (versus standard antidiabetic treatment) proved to be effective in reducing both epicardial and liver fat content in obese patients with type 2 diabetes; the effects were mainly weight loss dependent [92]. In another study, sitagliptin, a dipeptidyl-peptidase-4 inhibitor, also decreased the volume of EAT in a 24-week long study with obese type 2 diabetic patients [93]. Clearly, EAT should be considered as a novel therapeutic target, and statins, pioglitazone as well as incretin-based drugs are the best candidates so far [94, 95].

Conclusions

The epicardial fat is a unique fat compartment located between the myocardial surface and the visceral layer of the pericardium. The EAT can be quantified by non-invasive cardiac imaging techniques such as echocardiography, MRI or cardiac CT.

Among physiological determinants of EAT, age, gender, body weight and ethnicity should be considered. The EAT volume has a relatively strong genetic dependence, similarly to other visceral fat depots. Physiological functions of EAT may include protection of the myocardium against hypothermia and a mechanical protective role for coronary circulation. In addition, EAT may serve as a unique energy buffering pool in the homeostasis of the myocardium.

As for pathophysiological functions, it is widely accepted that EAT should be considered as a source of inflammatory mediators that might directly influence the myocardium and coronary arteries. In line with these observations, clinical studies suggested that EAT – through paracrine and vasocrine effects – may have an impact on the development and progression of coronary atherosclerosis. In addition, an association between increased EAT and atrial fibrillation was also documented. The insulin resistance syndrome (the metabolic syndrome), type 2 diabetes, NAFLD and CAD proved to be associated with an increased amount of epicardial fat. Interestingly, accumulation of EAT was also observed in patients with type 1 diabetes.

Treatment options for modifying EAT volume include lifestyle changes, bariatric surgery and using different drugs. Weight reduction in obese subjects may lead to a decrease in EAT volume, while effects of different drugs on EAT are controversial. Nevertheless, EAT should be considered as a new cardiovascular therapeutic target.

Conflict of interest

The authors declare no conflict of interest.

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