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Association Between Epicardial Adipose Tissue and Left Ventricular Strain in Patients with Type 2 Diabetes Mellitus

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Abstract:

Due to the rapid economic growth and ongoing enhancement of people's living conditions, the prevalence of diabetes mellitus type two (T2DM) is steadily rise, posing a significant risk to public health. Prior researches have shown that the cardiovascular (CV) problems associated with diabetes mellitus are the primary cause of mortality in people with diabetes mellitus type two. Superimposing Epicardial adipose tissue (EAT) is associated with coronary atherosclerosis and carotid atherosclerosis regardless of conventional cardiovascular risk factors. Due to its close connection with the myocardium, EAT has a direct impact on the function of cardiomyocytes. It is beneficial for the heart under normal conditions, but in a diseased state, it may release proinflammatory cytokines and produce oxidative stress. Speckle tracking echocardiography (STE) in two dimensions (2D) is an emerging imaging technique with great potential. Like tissue Doppler imaging (TDI), it enables the estimation of myocardial velocities and deformation characteristics such as strain and strain rate (SR) after the fact. These characteristics are widely acknowledged to provide valuable insights into the systolic and diastolic function, ischemia, myocardial mechanics, and several other pathological processes of the heart.

Keywords: left ventricular (LV) strain, Epicardial adipose tissue, T2DM

1. Introduction

The current understanding of the mechanism behind cardiovascular complications in DM involves several factors, including oxidative stress, the buildup of advanced glycoxidation end products due to elevated levels of blood sugar, insulin resistance (IR), increased metabolism of fatty acids, excessive calcium levels in heart muscle cells, and abnormalities in the renin angiotensin system[1].

Aside from the well-recognized causes, there has been a growing attention on the impact of (EAT) on the cardiovascular system in recent times. Epicardial adipose tissue is a metabolically active kind of visceral fat that develops from the mesoderm layer between the

heart and the visceral pericardium. There is increasing evidence to suggest that EAT has been recognized as a potential CV risk factor**[2].**

At present, there is an increasing amount of information indicating that excessive consumption of food is also linked to impaired functioning of the left ventricle in various illness conditions**[3].**

This work aimed to examine the correlation between EAT and LV strain in cases had T2DM.

Diabetes Mellitus Type two

T2DM is a disorder in which there is an imbalance in the way the body processes carbohydrates, lipids, and proteins. This happens because of a decrease in the insulin creation, a hormone that regulates blood sugar levels, or a reduced response to insulin, or both. Diabetes mellitus type two is far more prevalent, accounting for more than ninety percent of all occurrences, compared to T1DM or gestational diabetes. In recent decades, our comprehension of the formation and advancement of Diabetes Type two has undergone tremendous evolution. The primary factor behind this condition is the gradual decline in the Capacity of β-cells of the pancreas to create insulin, often occurring with IR which is pre-existing in liver, fat tissue, and skeletal muscles (SKM) [4].

Epidemiology

The CDC's National Diabetes Statistics Report states that the crude prevalence of diabetes in the adult people of the US is 14.7 percent. The occurrence of diagnosed diabetes among the adult population is 11.3 percent, whereas the prevalence of undiagnosed diabetes is 3.4 percent. The frequency of diabetes increases with advancing age, reaching a rate of 29.2 percent among those who are sixty-five or older. The data included in the research were extracted from the years 2017 to 2020[5]**.**

T2D mostly affects those who are forty years of age or older, and its occurrence becomes more prevalent as individuals age. Undoubtedly, the rising prevalence of T2D may be attributed, at least in part, to the aging of the population. The overwhelming majority of DM cases in elderly adults are classified as type 2[6]**.**

Pathophysiology

T2D is defined by the presence of both peripheral IR and insufficient insulin generation by β-cells of the pancreas. IR, caused by high amounts of proinflammation cytokines and fatty acids(FA) in the bloodstream, cause reduced glucose uptake by muscles, increased glucose production by hepatic cells, and enhanced breakdown of fat[7]**.**

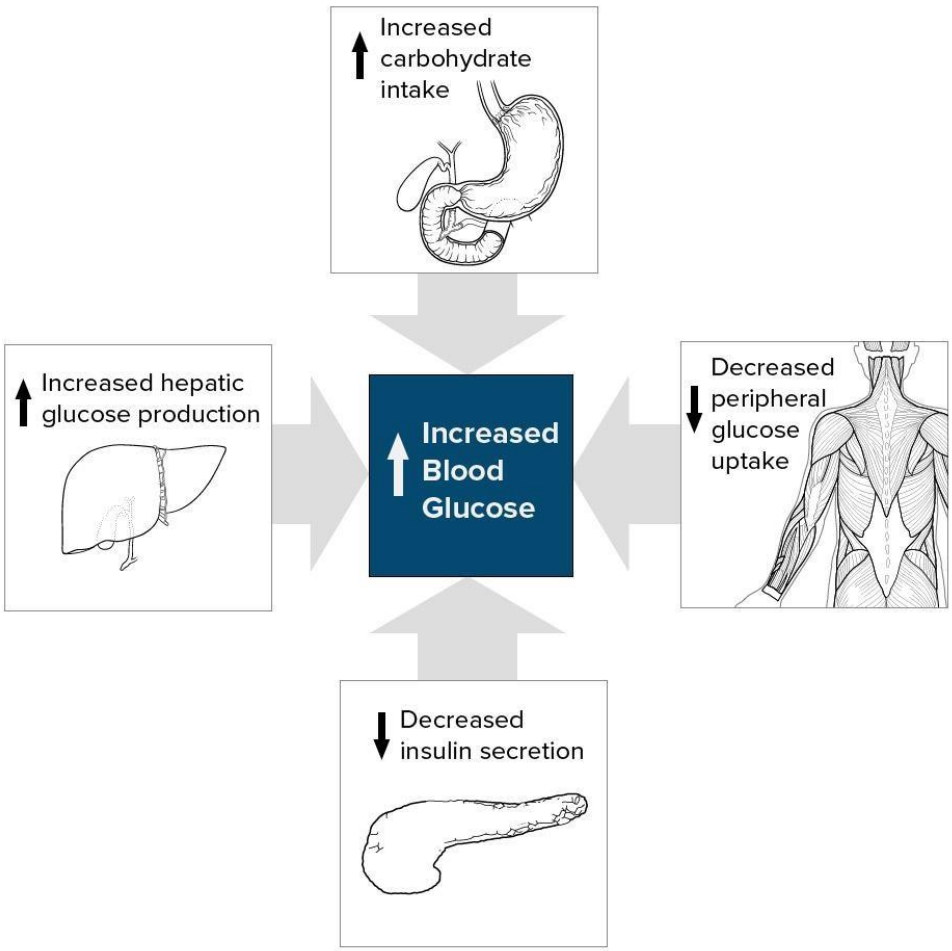

Figure (1): Simple scheme for the pathophysiology of diabetes type two [8].

Beta-cell disfunction

Beta-cell disfunction is a significant reason in prediabetes and diabetes, with research by Bacha et al confirming this in obese adolescents. It emerges at an early stage of the pathological process and is not always subsequent to phases of insulin resistance. The focus is shifting towards early beta-cell pathology treatment options.[9]**.**

Insulin resistance

Postprandial blood glucose levels first rise throughout the change from normal to abnormal glucose tolerance, ultimately resulting in fasting hyperglycemia. Insulin resistance may be developed by steroid use, high-calorie meals, or physical inactivity, increases glucagon and GIP levels, but the postprandial GLP-1 response remains unchanged [10]**.**

Genomic factors

Genome-wide association researchers have discovered genetic differences, known as single-nucleotide polymorphisms (SNPs), which are correlated with beta-cell activity and insulin resistance. These studies have revealed more than forty distinct loci in the genome that indicate a higher susceptibility to T2D.

Cardiovascular disease in T2DM

T2D cases have a greater risk of cardiovascular disorder (CVD) mortality than their age-matched counterparts. They are more likely to experience stroke events, myocardial infarction, CHD, angina pectoris, and sudden death. A significant percentage of individuals diagnosed with T2D experience mortality within one year after an acute myocardial infarction (MI), and many die outside the hospital. Female patients have a greater risk for CHD, Perhaps because of a greater load of risk factors and a stronger Ipact of blood pressure and atherogenic dyslipidemia.[11]**.**

Multiple researches indicate that cases with reduced glucose tolerance, characterized by 2-hour plasma glucose levels ranging from 7.8 to 11.0 millimole per liter, or impaired fasting glucose (IFG), characterized by plasma glucose levels ranging from 5.6 to 6.9 millimole per liter, have almost double the risk of CV disorder in comparison to those with normal blood sugar levels [12]**.**

Impaired endothelial function

Atherosclerotic lesions are primarily caused by impaired endothelial function, closely linked to insulin resistance. Insulin's vasodilatory action relies on nitric oxide generation, which can be reduced by hindering insulin-induced blood flow with nitric oxide generation inhibitors. nitric oxide -dependent rises in blood flow to SKM could represent 25-40% of glucose uptake in reaction to insulin stimulus.[13]**.**

Insulin-stimulated glucose uptake relies on signaling pathways that involve PI 3-kinase, phosphoinositide-dependent kinase 1, insulin receptor substrate 1 (IRS-1), Akt, and downstream effectors. These mechanisms contribute to the movement of insulin-responsive GLUT4 in response to insulin. Activation of PI 3-kinase is required for the generation of NO in response to insulin, but it alone is not enough to cause vasodilation. The Shc/Ras/mitogen-activated protein (MAP) kinase pathway is a separate component of the insulin-signaling pathway that controls the release of endothelin-1, a powerful vasoconstrictor, and vascular cell adhesion molecule 1 (VCAM-1) in the endothelium. It also regulates mitogenesis and growth. Metabolic IR is marked by a specific impairment in PI 3-kinase-dependent signaling, which is caused by proinflammatory cytokines like interleukin (IL)-1β, tumor necrosis-α (TNF-α), C-reactive protein (CRP), and IL-6. This impairment can lead to an imbalance among the production of nitric oxide (NO) and Glucose absorption in the endothelium, leading to IR and endothelium dysfunction [14]**.**

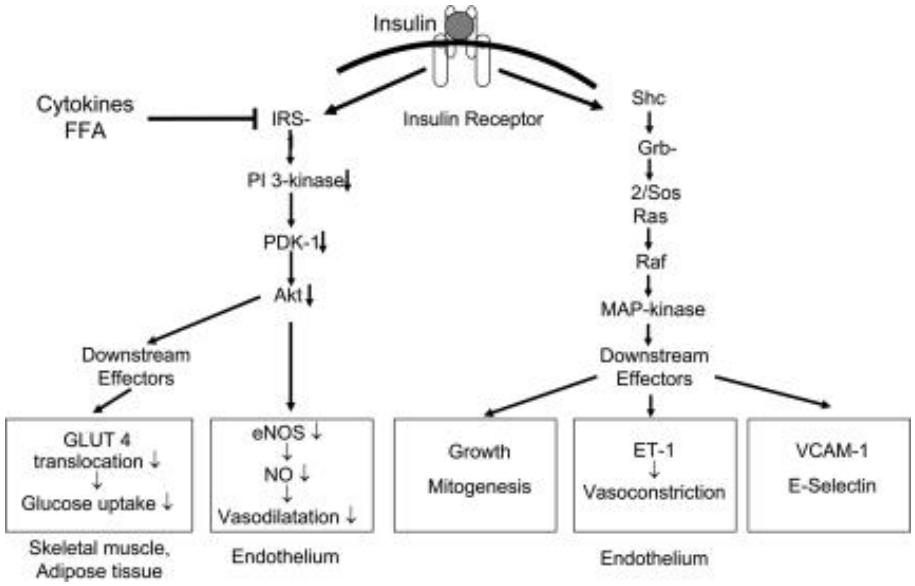

Figure (3): Insulin-signaling mechanisms that run parallel to each other have a role in both metabolic and circulatory impacts in peripheral tissues. eNOS refers to endothelial NO production, whereas endothelin 1(ET-1) [15]**.**

Subclinical inflammation

Insulin resistance is linked to type 2 diabetes, with insulin signaling pathways being closely linked. Adipose tissue secretes mediators and cytokines like leptin, interleukin -6, adiponectin, and tumor necrosis-α, which have an impact on inflammation, insulin resistance, and atherosclerosis. Obesity is linked to widespread inflammation in the body, which involves the presence of inflammatory proteins in the bloodstream. Cytokines of Inflammation like tumor necrosis-α ,interleukin -1β, and CRP stimulate the development of adhesion molecules [16]**.**

Adipokines

Adipokines like leptin, tumor necrosis-α, resistin, interleukin -6, visfatin, adiponectin, and retinol-binding protein 4 are linked to IR. Adiponectin, abundant in adipocytes, has antidiabetic, anti-atherogenic, and anti-inflammatory characterization. High adiponectin levels correlate with high insulin sensitivity. It inhibits vascular cell adhesion molecule 1, ICAM-1, and E-selectin expression, promoting anti-inflammatory and antiatherogenic characterization.[17]**.**

Atherogenic dyslipidemia

IR and T2D are linked to changes in lipoproteins and lipids. IR individuals have elevated levels of both total and very LDL triglycerides, while also displaying lower levels of HDLC in comparison to persons with high insulin sensitivity. Patients with T2D often exhibit increased concentrations of triglyceride-rich lipoproteins and reduced levels of HDLC[18]**.**

Thrombosis and fibrinolysis

DM and IR are linked to prothrombotic risk and fibrinolysis suppression due to elevated PAI-1 concentrations. IR conditions lead to reduced endothelial function, which hampers the formation of nitric oxide, synthesis of prostacyclin, and aggregation of platelets.

Hyperglycemia and glycation have a role in the formation of blood clots that are difficult to dissolve. PAI-1 levels are not influenced by obesity or poor glycemic management [16].

Diagnosis

The diagnostic criteria for DM have typically been based on glucose amount in blood. In recent times, HbA1c was included as a comprehensive indicator of long-term blood sugar levels (the average lifetime of a RBC is around One Hundred and Twenty d). Nevertheless, the process of haemolysis, which shortens the lifetime of red blood cells, might render HbA1c an unreliable metric. Additionally, advanced age, racial background other than white, excessive consumption of dietary fat, alcohol use, smoking, liver illness, renal disease, and iron deficiency may all have an impact on HbA1c levels, regardless of blood sugar levels [19]**.**

Screening

Screening for a serious disorder is suitable when the natural course of a condition is comprehended, it becomes possible to identify it at its pre-clinical phase, suitable, fast, cheap, valid, early management is more efficient, and screening enhances outcomes. T2D fulfills these requirements, and in 2014, the US Preventive Services Task Force recommended monitoring for impaired blood glucose amount and T2DM in adults over 45, obese cases, and those who had a 1st-degree relative with diabetes. Racial and ethnic minority groups are at elevated risk in comparison to whites. Other professional societies of diabetes recommend opportunistic monitoring for T2D in primary care strategies.[20]**.**

Management

By making changes to one's lifestyle and dietary habits. Research has demonstrated a substantial decrease in the occurrence of diabetes mellitus type 2 when cases maintain a BMI of 25 kilogram per square meter, consume a diet has high fiber and unsaturated fats while avoiding saturated and trans-fats and foods with a high glycemic index, engage in regular physical activity, refrain from smoking, and consume alcohol in moderation. Proposing that a significant proportion of diabetes mellitus type two may be averted via changes in one's lifestyle. Patients diagnosed with diabetes mellitus type two should undergo a medical nutrition assessment. Lifestyle suggestions must be customized based on their functional and physical capacity[21]**.**

Pharmacological Agents

Biguanides

Metformin, a frequently prescribed biguanide for overweight and obese individuals, blocks the production of glucose in the hepatic cells, improves the body's response to insulin, promotes the uptake of glucose, boosts the FAO, and decreases the glucose absorption. In 2008, research demonstrated that metformin stimulates the activation of AMP-activated protein kinase, an enzyme that has a crucial function in gene expression involved in the production of glucose in the liver. Given the potential risk of lactic acidosis, it is advisable to use caution while administering this medication to older cases with diabetes and impaired kidney function. Metformin has a reduced occurrence of hypoglycemia in comparison to sulfonylureas[22]**.**

Sulfonylureas

Sulfonylureas, which stimulate insulin secretion, can elevate hypoglycemia probability in Old cases with diabetes type two. Glyburide is related to greater hypoglycemia incidences in

comparison to glipizide. Risk factors for this condition include decreased kidney function due to aging, concurrent use of insulin, being over the age of 60, recent release from the hospital, alcohol misuse, restricted calorie intake, and using many drugs. Elderly cases should avoid using long-acting sulfonylureas such as glyburide and instead opt for short-acting glipizide.[21]**.**

Meglitinides

Nateglinide and repaglinide are non-sulfonylurea secretagogues that activate insulin generation from β-cells of pancreas through the ATP-dependent K-channel. Meglitinides, with a fast onset and short action period, are taken before eating for postprandial blood glucose management. Taking of the therapy before eating permits flexibility in case of forgotten meals without rise in hypoglycemia risk. Repaglinide undergoes mostly hepatic metabolism, with limited renal excretion, making dosage modification unnecessary in cases with kidney impairment.[23]**.**

Thiazolidinediones

Thiazolidinedione is an insulin sensitizer used to address IR in type two diabetes patients. It is now mainly used in the treatment of pioglitazone, which has been restricted by the FDA due to increased cardiovascular events. Pioglitazone is well tolerated in older adults and can be utilized in patients of renal disfunction. However, its use can be limited because of concerns about fluid retention, peripheral edema, and fracture risk in women. It is also contraindicated in old patients with congestive heart failure and heart failure class three-four.[24]**.**

Alpha-Glucosidase Inhibitors

Acarbose, Voglibose, and Miglitol are potentially safe and effective treatments for type 2 diabetes, particularly postprandial hyperglycemia. However, they must be inhibited in cases had kidney disfunction because of side-effects like flatulence and diarrhea. Voglibose, the latest drug, was found to enhance tolerance of glucose, delay illness development, and increase patients achieving normal glucose level.[25]**.**

Incretin-Based Therapies

Glucagon-like peptide 1 (GLP-1) analogs serve as the basis for incretin-based medicines, aiming to address this hitherto unidentified aspect of diabetes pathogenesis, leading to long-lasting improvements in glycemic management and better management of weight of body. These medications may be used alone, with diet and exercise, or in conjunction with hypoglycemic medicines taken orally in cases who have diabetes type 2. Two examples of drugs in this category are Exenatide, which is an incretin mimic, and Liraglutide [26].

The use of GLP-1 treatments does not pose a danger of hypoglycemia, unless they are taken with insulin secretagogues. Furthermore, recent findings indicate that incretin-based medicines may have a beneficial influence on inflammation, hepatic and cardiovascular well-being, the CNS, and sleep [26].

Dipeptidyl-Peptidase IV(DPP-4) Inhibitors

DPP-4 inhibitors are a new class of anti-diabetogenic medications which inhibit dipeptidyl peptidase-4 (DPP-4), an enzyme that inactivates GIP and Glucagon-like peptide 1, improving islet function and glycemic control in diabetes type two. These drugs are effective as alone or in mix with metformin, insulin, and thiazolidinediones. These medications have a high level of tolerance, have a low risk for hypoglycemia, and do not cause weight gain. Nevertheless, they

are comparatively costly and the lasting impact on glycemic management and beta-cell activity has yet to be determined [22].

Insulin

Insulin is administered either on its own or in conjunction with oral hypoglycemic medications. Enhancement treatment with basal insulin is beneficial for preserving β-cells function, but replacement therapy is necessary for beta cell depletion. Glucose poisoning necessitates the use of alternate treatment for rescue purposes. Injectable versions of insulin are available in several types, such as fast-acting, short-acting, moderate-acting, and long-acting. Long acting insulin is less prone to causing decrease in glucose.[27].

Insulin analogues

Insulin therapy has limitations in replicating normal production of insulin. Traditional moderate- and long-acting insulins (lente insulin, ultralente insulin, and NPH insulin) have inconsistent uptake and peaks of action, which can lead to hypoglycemia. The new analogs of insulin have different pharmacokinetic characterizations in comparison to regular insulins, with varying onset and action period. Currently, there are 2 rapid-acting insulin analogs (insulin lispro and insulin aspart) and one extended-acting insulin analog (insulin glargine) that can be obtained [28].

Future in Drug Therapy Inhaled Insulin

In 2006, the inhaled version of quickly acting insulin was authorized by both FDA and the European Medicines Evaluation Agency for the management of diabetes type one and type two in adults. This is a fast-acting kind of insulin that is used in individuals with diabetes type one and type two. It has the benefit of being delivered straight into the lungs. Researches have demonstrated that insulin by inhalation is equally effective as, but not superior to short-acting insulin. The manufacturer discontinued the product in October 2007 due to low sales [23].

Bromocriptine

Quick-release Bromocriptine is a newly discovered medication for managing diabetes type two . Nevertheless, the precise mechanism of action remains unclear. Research has shown that after 24 weeks of treatment, they may decrease the average HbA1c levels by zero percent to 0.2 percent [29].

Others

Compounds that block SGLT-2, leading to increased removal of glucose by the kidneys, and compounds that inhibit 11ß-hydroxysteroid dehydrogenase 1, reducing the impacts of glucocorticoids in the hepatic cells and fat tissue.

Researchers are now evaluating insulin-releasing glucokinase activators, pancreatic-G-protein-coupled FA-receptor agonists, metabolic inhibitors of hepatic glucose output, and glucagon-receptor antagonists as potential novel pharmacological therapies for type two diabetes cases [30].

Epicardial adipose tissue and left ventricular strain in type 2 DM

Anatomy and physiology of EAT

EAT is a fat deposit situated between epicardium and myocardial. It is nourished by Coronary artery branches. Conversely, pericardial adipose tissue (PAT) is situated outside and receives its blood supply from arteries that are not part of the coronary circulation. Epicardial adipose tissue is commonly found in the interventricular and atrioventricular grooves. It may be classified into two types: pericoronary Epicardial adipose tissue, which is positioned immediately surrounding or on the outer layer of the coronary artery, known as adventitia, and myocardial EAT, which is the fat depot found just above the heart [31]**.**

The function and appearance of the epicardial adipose tissue undergo alterations as cases age and in the presence of pathological situations. Notably, both intra-abdominal and epicardial fat depots originate from brown fat cells. epicardial adipose tissue is believed to provide heat directly to the myocardial and safeguard the heart under adverse hemodynamic circumstances, like ischemia. The mechanisms involved in regulating thermogenesis in epicardial adipose tissue are complex and yet not completely understood. In newborns, epicardial adipose tissue exhibits characteristics and behaviors similar to brown fat, but with restricted physical adaptability and sensitivity to external stimuli [32]**.**

In advanced coronary artery disease (CAD), The expression of EAT genes, which encode proteins involved in the process of adipocyte browning and thermogenic activation, is decreased, while pro-inflammatory cytokines are increased. This could be due to fibrosis and apoptosis in EAT. Nevertheless, it is possible to stimulate EAT to restore its brown fat-like functionality, providing heart benefits in cases with long-term ischemic conditions. More researches are needed to assess EAT's adaptability to different metabolic disorders (**Peterson et al., 2019).**

Targeting EAT in cardiovascular disease

Epicardial adipose tissue is a modifiable CV risk factor and a possible new target for therapeutic intervention due to its reactivity to medicines with pleiotropic impacts like GLP-1 receptor agonists and GLP-1 receptor inhibitors. Cardiovascular outcomes studies have shown that medicines including GLP-1 receptor agonists and SGLT2i decrease the occurrence of severe CV events. The observed effect sizes indicate that these medications involve mechanisms that go beyond just improving glycaemic control, however these mechanisms have not been completely understood[33]**.**

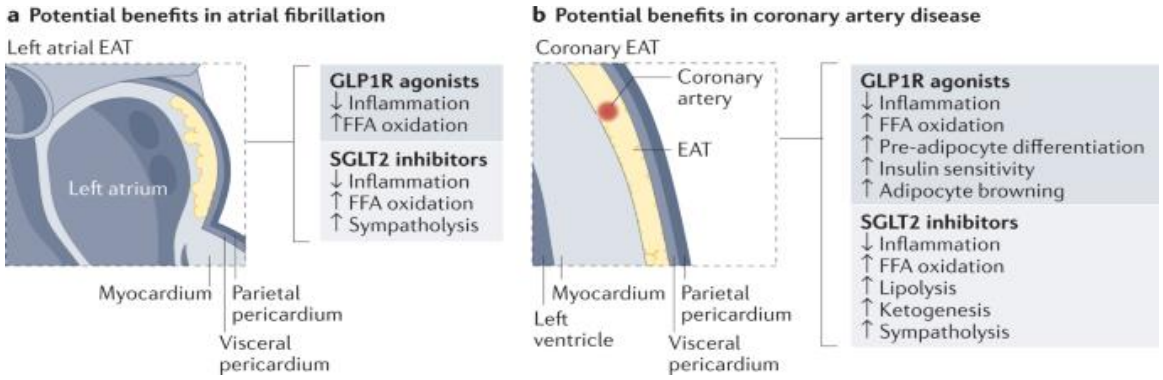

Figure (5): Targeting EAT with GLP1 receptor agonists and SGLT2i [31].

The potential positive benefits on heart and metabolic health of SGLT2 inhibitor and glucagon-like peptide 1 receptor (GLP1R) agonist therapy go beyond their impact on blood sugar levels and blood flow. SGLT2i and GLP-1 receptor agonists may specifically target both the fat cells around the left atrium (known as left atrial epicardial adipose tissue) and the fat cells surrounding the coronary arteries. This targeted approach can be used for the management and inhibition of AF (part a) and coronary artery disorder (part b), correspondingly. Both SGLT2i and GLP1R agonists have the ability to decrease inflammation in epicardial adipose tissue and enhance the utilization of free fatty acids (FFAs) as a source of energy for the heart muscle. Additionally, glucagon-like peptide 1 receptor agonists promote the conversion of white fat to brown fat and the differentiation of pre-adipocytes, resulting in improved insulin sensitivity in the heart muscle. These effects collectively contribute to the enhancement of myocardial metabolism. SGLT2 inhibitors may cause a decrease in sympathetic activity and an increase in the breakdown of fats in epicardial adipose tissue, leading to a rise in the production of ketones and a reduction in oxygen consumption in cases with heart failure.

glucagon-like peptide 1 receptor agonists are injectable drugs used to treat diabetes type 2 and obesity. They have cardiovascular advantages that go beyond controlling glucose levels. One of the proposed non-glycaemic benefits of the glucagon-like peptide 1 receptor agonist liraglutide is the decrease of visceral fat. Among cases with diabetes type 2 and obesity, the glucagon-like peptide 1 receptor agonists liraglutide (administered daily), semaglutide (administered weekly), and dulaglutide (administered weekly) exhibit a more pronounced reduction in epicardial adipose tissue thickness compared to the total decrease of body weight. Epicardial adipose tissue specifically expresses glucagon-like peptide 1 receptor , but subcutaneous fat does not. Hence, the existence of glucagon-like peptide 1 receptor in Epicardial adipose tissue substantiates the theory of a direct impact on the fat reservoir. Stimulating Epicardial adipose tissue GLP-1R may decrease the formation of fat cells in a specific area, enhance the use of fat, promote the development of brown fat, and regulate the renin-angiotensin-aldosterone system. The metabolic alterations might potentially contribute to the beneficial impact of glucagon-like peptide 1 receptor agonists on the cardiovascular system. Notably, glucagon-like peptide 1 receptor is also present in human cardiomyocytes [34].

Myocardial insulin-mediated glucose absorption and mitochondrial oxidative metabolism are compromised in cases of heart failure. The dysfunctional heart decreases the oxidation of FA and glucose, while increasing the consumption of ketones by the heart. The use of SGLT2i medication promotes the oxidation of ketone bodies, namely β-hydroxybutyrate, which therefore becomes the primary and alternate source of energy in place of glucose and fatty acid oxidation (FAO). This substrate selection enhances oxygen consumption, resulting in improved cardiac function at the mitochondrial level due to the decreased energy expenditure associated with β-hydroxybutyrate oxidation in comparison to pyruvate and glucose oxidation. Epicardial adipose tissue might potentially act as an intermediary for the non-glycosuric cardiovascular effects of SGLT2i. Yes, SGLT2 inhibitors may stimulate the metabolism of epicardial adipose tissue and help enhance the metabolism of the heart muscle. The consumption of food is a significant provider of FA and lipids. If consumed excessively and stored, these substances may penetrate the underlying myocardial and contribute to the development of heart failure [35].

Thus, SGLT2i, such as empagliflozin and dapagliflozin, have the potential to decrease the amount of fat stored within the heart muscle by promoting the metabolism of fat in the epicardial adipose tissue and the use of ketone bodies. While the cardiovascular benefits of

Epicardial adipose tissue might lipolysis caused by sodium–glucose co-transporter 2 inhibitor medication haven't yet been shown, we may speculate on plausible pathways based on available evidence. The expression of cardiac fatty acid-binding protein (FABP3) is increased in epicardial adipose tissue of individuals suffering from heart failure. fatty acid-binding protein facilitates the movement of increased levels of FA that are generated during lipolysis in epicardial adipose tissue and carries them to the neighboring heart. Insulin sensitivity has a significant impact on the process of fatty acid oxidation. Research has shown that dapagliflozin may enhance insulin sensitivity and the absorption of glucose. Thus, the enhanced cardiac metabolism of glucose and insulin sensitivity caused by SGLT2i might enhance the consumption of FA [36].

Medical imaging techniques utilized for estimating EAT

Presently, three imaging modalities are often used for evaluating Epicardial adipose tissue , including computed tomography , echocardiography and MRI. In 2003, Iacobellis et al. [37] first suggested using transthoracic echocardiography to quantify the thickness of epicardial adipose tissue on the right ventricle's free wall. They also highlighted that EAT thickness might serve as a novel marker for stratifying cardiovascular risk. Echocardiography quickly emerged as the predominant technique for measuring EAT due to its widespread availability and affordability. Nevertheless, as highlighted by various academics, this approach has some limitations. Echocardiography does not provide a comprehensive measurement of the overall volume of epicardial adipose tissue . Instead, it only evaluates the thickness of EAT at specific places. Due to the uneven distribution of Epicardial adipose tissue across patients, EAT thickness is a less dependable indicator of the quantity of EAT in comparison to Epicardial adipose tissue volume. Therefore, there is a more pronounced correlation between the amount of epicardial adipose tissue and the development of cardiovascular disorder. Furthermore, the use of echocardiography is currently limited due to its incapacity to distinguish between epicardial and pericardial adipose tissue. Furthermore, the repeatability and accuracy of echocardiography is worse compared to CT-based approaches [38].

Increased EAT in obese or diabetic cases suggests a higher CVD risk

Multiple researches have shown a robust linear correlation between the Epicardial adipose tissue amount and the occurrence of obesity. Moreover, individuals diagnosed with diabetic mellitus type 2 had considerably greater thickness and volume of EAT. Moreover, an elevated EAT is sometimes a sign of newly developed diabetes mellitus.

Kang et al. [39] conducted a retrospective analysis and discovered that cases who had a baseline Epicardial adipose tissue thickness of ≥5 millimeters had a much greater likelihood of acquiring diabetes. Epicardial adipose tissue is further linked to other constituents of metabolic syndrome (MetS). Multiple studies have shown a direct correlation between the quantity of Metabolic Syndrome components and the thickness of Epicardial Adipose Tissue. The indicator Epicardial adipose tissue is thought to be beneficial in assessing the risk of getting metabolic syndrome as well [39]**.**

An enlarged epicardial adipose tissue was proposed to result in the progression of cardiovascular disorders and elevated mortality rates in individuals with diabetes. Wang et al. conducted a logistic regression study and discovered a significant association between the volume of epicardial adipose tissue and the Gensini score, coronary lesions, and coronary calcium scores in cases with diabetes type 2. Similarly, a prospective trial including two

hundred cases with diabetes type 2 but no known coronary artery disorder found that a large amount of epicardial adipose tissue was associated with a higher likelihood of developing coronary artery disorder following a period of six years of observation. Previous studies have shown comparable results [40]**.**

The quantity of EAT is linked to reduced myocardial systolic performance, even when the 3D left ventricular ejection fraction is intact and there is no obstructive coronary artery disorder. This recommends that EAT may have a substantial role in the development of heart disease in cases with obesity, diabetes, and metabolic disorders [41].

Mounting data has unequivocally shown that the quantity of epicardial adipose tissue is elevated in individuals who are obese and have diabetes. Among cases with diabetes, a greater amount of EAT is associated to a heightened susceptibility to cardiovascular disorders and worse cardiac diastolic function. However, further comprehensive research are required to determine if T2D exacerbates the disease-causing capabilities of EAT and whether EAT contributes to the acceleration of cardiovascular disorders development in DM cases [41].

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