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Obesity and Metabolic Syndrome: Pathophysiological Mechanisms Driving Cardiovascular Risk

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Abstract

Obesity and metabolic syndrome have become a significant public health issue, which has led to increasing rates of cardiovascular disease morbidity and mortality. This narrative review provides an overview of the most recent evidence (2017–2024) to update the underlying pathophysiological discussion on the relationships between adipose tissue dysfunction, chronic inflammation, insulin resistance, and ectopic lipid deposition, leading to the development of hemodynamic stress, endothelial dysfunction, and structural cardiac remodeling. Central pathophysiological derangements include adipokine dysfunction, lipotoxic injury from ceramides and diacylglycerols, and neurohormonal activation of the renin-angiotensin-aldosterone and sympathetic nervous systems. These processes lead to a variety of cardiovascular phenotypes, such as heart failure with preserved ejection fraction (HFpEF), arrhythmias, atherosclerosis, and sudden cardiac death. From the clinical perspective, obesity increases diagnostic difficulties due to imaging artifacts of the epicardial fat and overlapping symptoms of HFpEF, so advanced biomarkers and individualized diagnostic methods are required. Novel approaches (lifestyle intervention, anti-diabetic drugs such as SGLT2 inhibitors, GLP-1 agonists, and bariatric surgery) have effectively reduced cardiovascular risk by acting on metabolic abnormalities, inflammation, and cardiac adaptation. The review signals the need for multifaceted care delivery models to integrate metabolic with cardiovascular risk management and the necessity for public health efforts to stem the tide of obesity and lead to equitable therapy access. Upcoming studies should focus on molecular mechanisms of cross-talk between the adipose and the organ system level and improve

risk stratification tools to counteract the ongoing avalanche of obesity-associated cardiovascular disease.
Key words: Obesity cardiomyopathy, insulin resistance, adipokines, SGLT2 inhibitors, HFpEF.

Section 1: Introduction

Global Burden of Obesity

Obesity is ranked as the fifth leading cause of global mortality, resulting from an energy imbalance between caloric intake and expenditure [1]. Over the past 50 years, obesity prevalence has sharply increased worldwide [2].

European Association for the Study of Obesity 2023 statistics state that there are already over 1 billion obese people globally, including 650 million adults, 340 million adolescents, and 39 million children [1]. The World Health Organization emphasizes that a person is considered overweight if their Body Mass Index (BMI) is 25 to 29.9 and obese if their BMI is 30 or above [1]. According to the World Obesity Federation's 2023 Atlas report, by 2035, over half of the world's population will either be overweight or obese, and about 2 billion people will be obese [3].

Metabolic syndrome was defined in 2009 with hypertension, dyslipidemia, raised fasting glucose, and central Obesity as abnormal findings [4]. A research investigation conducted from January 2022 to February 2023 showed the prevalence of metabolic syndrome as 63.3% [5].

Obesity and Cardiovascular Risk

The severity of Obesity influences the pathophysiology of numerous metabolic diseases, especially diabetes, hypertension, and dyslipidemia. Obesity is also an independent risk factor for ASCVD, heart failure, and aortic stenosis [6]. Due to its association with atherogenic characteristics, abdominal Obesity raises the risk of heart attacks and strokes at an earlier age [7]. The constellation of risk factors associated with metabolic syndrome has multiple pathophysiological implications, such as endothelial dysfunction, atherogenesis, thrombosis, myocardial injury, fibrosis, and cardiac remodeling. MetS affects several subtypes of CVD, including heart failure, peripheral artery disease, cardiac arrhythmias, coronary heart disease, and cerebrovascular illness [8].

Adipose Tissue in CVD Pathogenesis

Lipids are primarily stored in the body's major endocrine organ, white adipose tissue [9]. Adipose tissue also secretes adipokines, a cytokine class that affects the body's metabolism, endocrine function, and inflammation [10]. When caloric intake consistently exceeds energy expenditure, adipose tissue expands via hypertrophy and hyperplasia. This results in Obesity and is associated with other systemic metabolic issues, like inflammation, substantial tissue remodeling, and insulin resistance [11].

This narrative review aims to discuss the mechanistic pathways by which obesity and metabolic syndrome contribute to CVD, including adipose tissue dysfunction, chronic inflammation, and insulin resistance, and their clinical implications. It also summarizes novel therapeutic approaches and diagnostic problems for actionable implications for clinicians and researchers.

Importance of this review

The global prevalence of obesity and its cardiovascular complications has reached pandemic proportions, yet gaps persist in synthesizing recent advances in pathophysiology, diagnostics, and therapeutics. Molecular mechanisms, such as adipokine dysregulation and lipotoxicity are usually not included in current reviews which do not link them to clinical outcomes (e.g., HFpEF) nor discuss novel therapies (such as SGLT2 inhibitors and GLP-1 agonists). This review fills that void, linking basic science findings with translational and population-level implications to provide a comprehensive view of obesity and CVD.

Section 3:Pathophysiology

Adipose tissue dysfunction

Adipose tissue is an active endocrine organ; it was at one time considered merely a site for storing fat. Adipose tissue gains dysfunctionality in Obesity and acquires the anomaly of hypertrophy in adipocytes with fewer preadipocytes generated and downregulation of peroxisome proliferator-activated receptor gamma (PPARγ) expression, laying the basis for insulin resistance [12]. Hypertrophic hypoxic adipocytes induce acute and chronic inflammatory conditions, along with extracellular matrix remodeling. The ability of the adipocyte to accumulate triglycerides then becomes saturated, and using that, fat is deposited ectopically in the liver, muscle, and heart. This phenomenon causes systemic metabolic dysregulation [13,14].

Inflammation and Adipokine Dysregulation

Obesity-induced dysfunction of adipose tissue disturbs the secretion of adipokines. The threshold of proinflammatory signaling that is detected by adipocytes via adiponectin. There is also a diminished concentration of the anti-inflammatory adipokine, adiponectin, and an augmented proinflammatory cytokine (e.g., TNF-α, IL-6, and MCP-1) [15]. Elevated cytokines prevent insulin signal transduction, attract more macrophages, and produce chronic low-grade inflammation, which can cause insulin resistance, endothelial dysfunction, and atherosclerosis [16,17,18].

Insulin Resistance and Lipotoxicity

Inflammation, endoplasmic reticulum stress, and ectopic deposition of specific lipids, including ceramides and diacylglycerols, are reasons for insulin resistance [13,19]. Insulin resistance in the liver causes increased hepatic glucose production and decreased glucose storage as glycogen = resulting in high blood sugar. Thus, glucose uptake will be reduced in the skeletal muscle. Lipotoxicity compounds the metabolic insult by altering insulin signaling and induction of apoptosis and inflammation in hepatic and cardiac tissue [19].

Cardiovascular Consequences

Insulin resistance, inflammation, and dyslipidemia will all harm cardiovascular health. ED due to oxidative stress and reduced NO will initiate atherosclerosis. Dyslipidemia, high triglycerides, low HDL-C, small dense LDL, plaque development, and vascular wall injuries will be exacerbated [20]. The

injurious, inflammatory, and lipotoxicity that ensues will eventually lead to cardiac steatosis, hypertrophy, and heart failure [21].

Liver Disease: NAFLD/MASLD

NAFLD, also known as metabolic dysfunction-associated steatotic liver disease (MASLD), results from lipid accumulation in the liver secondary to insulin resistance and enhanced lipogenesis or de novo lipogenesis [22]. The "two-hit hypothesis" is a proposed mechanism for the pathophysiology of NAFLD. Fat deposits also make the liver more susceptible to oxidative stress and inflammation, which consequently causes steatohepatitis, fibrosis, and cirrhosis [18]. The toxic lipids act as mediators of mitochondrial function and cause apoptosis of hepatocytes.NAFLD/MASLD is also an independent risk factor for CVD.

Clinical Implications

The treatment of Obesity and MetS is associated with lifestyle changes focused on either weight loss or metabolic health. Pharmacologic treatments(e.g., GLP-1 agonists, SGLT2 inhibitors, and PPAR agonists) may be helpful adjuncts to these lifestyle changes. Increasing the understanding of adipose biology and molecular inflammation will help personalize treatment.

Section 4: Mechanisms Linking Obesity to Cardiovascular Disease

The worldwide increase in Obesity creates a significant health issue because it leads to higher chances of developing cardiovascular diseases (CVDs). Medical studies confirm this relationship by showing how hemodynamic changes, cardiac remodeling, and elevated clinical cardiovascular risk develop [23].

Hemodynamic Changes

When Obesity occurs, the body experiences significant hemodynamic changes, leading to elevated blood volume and cardiac output. The increased blood pressure levels and heavier workload on the left ventricle develop into hypertension because of these changes. Grandi explains that hypertensive cardiac remodeling occurs from chronic pressure overload, which leads to changes in heart structure and function [24]. The pathophysiological changes create conditions for multiple cardiovascular complications, including left ventricular hypertrophy and heart failure.

Cardiac Remodeling and Functional Changes

Obesity triggers cardiac remodeling, producing structural and functional changes in the heart. The increased hemodynamic stress causes the left ventricle to become thicker and results in poor heart muscle relaxation during diastole. The release of proinflammatory cytokines and adipokines from visceral adiposity worsens this process by directly affecting myocardial structure. Obesity speeds up the heart's normal aging process, resulting in premature cardiac dysfunction development [25]. The multifaceted effects of Obesity on heart structure and function result in both heart failure with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF) [26].

Clinical Cardiovascular Risk

A wide range of cardiovascular diseases, including coronary artery disease, stroke, and arrhythmias, exist as an independent and treatable risk factor because of Obesity. Research shows that Obesity leads to coronary heart disease regardless of other health conditions that may exist [27]. Type 2 diabetes mellitus often occurs alongside Obesity, which elevates cardiovascular risks, especially among elderly patients [28]. The combined effects of these associations result in elevated cardiovascular morbidity and mortality rates among obese populations.

The scientific evidence demonstrates that Obesity leads to cardiovascular diseases through blood pressure changes, hormonal effects, and heart structure modifications. Comprehending these mechanisms enables the development of preventive measures and effective management strategies to decrease the worldwide cardiovascular disease burden in obese people.

Section 5: Insulin Resistance and the Heart

Insulin resistance and Obesity set up the development of cardiovascular disease. Hypertrophic adipocytes cause insulin resistance and lipolysis, releasing non-esterified fatty acids into the bloodstream. They gather in the heart and liver and decrease nitric oxide production, developing vascular dysfunction [29]. Fat buildup forms harmful byproducts like ceramides, DAGs, and long-chain acyl-CoAs, which stimulate PKC isoforms that interfere with GLUT4 movement, aggravating hyperglycemia [30].

Hypertrophic adipocytes and immune cells release TNF-α, IL-6, and IL-1β, which destroy the endothelium and intensify insulin resistance. Concomitantly, adiponectin drops along with a rise in leptin and PAI-1, worsening inflammation [29]. Chronic inflammation elevates NF-κB, JNK, and JAK/STAT pathways, contributing to insulin resistance [31].

Typically, insulin aids vasodilation by nitric oxide production in activating the PI3K/Akt pathway. This pathway is inhibited in insulin resistance, leading to endothelial dysfunction, while MAPK remains active, stimulating vasoconstriction and vascular remodeling [29].

In the heart, insulin resistance disrupts glucose uptake IRS–PI3K–Akt pathway, playing a significant role in diabetic cardiomyopathy. The discovery of Rg3 shows it activates AMPK and helps reestablish the amount of insulin signaling proteins IRS-1, Akt, and AS160, all of which improve insulin sensitivity in cardiomyocytes [32]. Sulforaphane is shown to degrade p53, resulting in less TRIB3 and restoring insulin signaling [33]. ECM expansion with excess collagen and hyaluronan also impedes insulin sensitivity, as shown in MMP9 knockout mice, and causes heart stiffness. Drugs like PEGPH20 and pirfenidone undo this effect [34].

Diabetes worsens HF through both vascular and myocardial damage: hyperglycemia and ROS damage endothelial cells, while AGEs, mitochondrial dysfunction, calcium defects, and RAAS/SNS activation instigate fibrosis and hypertrophy [35]. Addressing heart issues in these patients goes beyond controlling hyperglycemia; it involves tackling a wide range of metabolic and structural heart problems [36]. Notably, SGLT2 inhibitors are key as they reduce heart failure risk compared to other drugs [37].

The TyG index can be a practical marker for insulin resistance and is helpful for cardiovascular risk assessment.

Section 6: Dyslipidemia and atherogenesis in metabolic syndrome

Dyslipidemia is extensively involved in both metabolic syndrome and ASCVD. Dyslipidemia in obesity shows increased LDL, triglycerides, non-HDL cholesterol, apolipoprotein B, and reduced HDL-C levels. Interestingly, it is not just the amount but also the quality of cholesterol that matters, as it shows that even low levels of LDL-C can increase plaque formation and atherosclerosis [4,38]. This dyslipidemia, which occurs due to insulin resistance, increases lipolysis and levels of free fatty acids, resulting in increased hepatic VLDL production [4,12]. Cholesterol ester transfer protein activity also rises, decreasing HDL-C and transforming LDL to sdLDL, promoting atherosclerosis [4,38,39]. The additional lipid insults that chronic low inflammation and endothelial dysfunction exert to worsen pathological vascular damage cannot be overestimated. In MetS, proinflammatory cytokines TNF-α, IL-6, and CRP contribute to endothelial dysfunction, activation, and vascular remodeling in a chronic period [4,40]. Oxidized LDL has been shown to impede nitric oxide bioavailability, induce the expression of ICAM, VCAM-1, and activate Rho-associated kinase signaling, causing inflammation and disrupting repair of the endothelium [41]. Lipoproteins rich in triglycerides worsen inflammation, and additionally, HDL loses its anti-inflammatory and anti-oxidant features, increasing cardiovascular risk. [41].

CRP, especially hs-CRP, is a biomarker and a mediator of vascular dysfunction in T2DM, inhibiting NO production and inducing immune activation and vascular remodeling via IL-6, TNF-α, and leptin signaling [40]. Insulin resistance, the hallmark of MetS, inhibits PI3K/Akt signaling, activating MAPK pathways that generate ROS and inflammatory effects driven by NF-κB [42,43]. Adipokines such as leptin and resistin activate cytokines and inflammasomes, aiding foam cell formation and plaque advancement [42].

The Ty-G index can help us predict the risk of heart failure [43]. By directly targeting interventions on lipid abnormalities, inflammation, insulin resistance, and autophagy, we may identify more precise approaches to lowering ASCVD risk in MetS and T2DM [4,39-44].

Section 7: Hypertension and vascular dysfunction

Hypertension and Obesity are closely interconnected. Obesity produces persistent activation of the RAAS, which causes sodium retention and vasoconstriction, exacerbating high blood pressure [45] In addition to that, increased adiposity results in increased levels of leptin in the blood. Leptin stimulates POMC neurons, activating the melanocortin-4 receptor pathway, resulting in increased SNS activity, increasing heart rate, vasoconstriction, and sodium retention, collectively increasing blood pressure [45].

More notably, adipose tissue causes resistant hypertension, which means high blood pressure despite the use of three or more antihypertensive drugs. This is caused by multiple factors like sodium

retention, activation of SNS and RAAS, and, interestingly, obstructive sleep apnea syndrome, which is common in Obesity [46]. Production of vasoconstrictors such as angiotensin II and leptin and a simultaneous decrease in vasodilators such as adiponectin and angiotensin 1-7 cause an imbalance that forms vascular stiffness [46]. Increased levels of inflammatory molecules such as TNF-α, IL-6, and IL-8 decrease nitric oxide, diminishing blood vessel relaxation and increasing oxidative stress [47].

Additionally, in Obesity, perivascular adipose tissue decreases vasodilators like NO, adiponectin, and angiotensin 1-7 and increases vasoconstrictors, especially angiotensin II and leptin. Proinflammatory cytokines cause insulin resistance and stop NO production, which leads to vascular dysfunction and stiffness. The Framingham Cohort studies show that increased PVAT is associated with arterial stiffness, so Obesity causes vascular dysfunction [47]. All these processes create a cycle of vascular thickening and narrowing, so weight loss is key to reducing cardiovascular risk [48]. **Table 1** summarizes the key alterations in adipokine and cytokine profiles associated with obesity-related cardiovascular dysfunction, including their direction of change and primary effects on the cardiovascular system

Table 1. Adipokine and Cytokine Alterations in Obesity-Related Cardiovascular Dysfunction

Adipokine/ Cytokine	Change in Obesity	Effect on Cardiovascular System	References
Adiponectin	↓	Loss of anti-inflammatory & anti-atherogenic effects	[15,29]
Leptin	↑	Increased Sympathetic Tone & RAAS Activation	[29,45]
Resistin	↑	Promotes insulin resistance & foam cell formation	[42]
TNF-α	↑	Endothelial activation, matrix remodelling	[15,40,47]
IL-6	↑	Induces CRP, drives chronic vascular inflammation	[4,15,40,47]
MCP-1	↑	Recruits monocytes/ macrophages to vessel wall	[15-18]

Section 8: Obesity cardiomyopathy, and Heart failure

Definition and Epidemiology

Interruption of structural, functional, and electrical physiology of the heart in long-standing obese individuals, irrespective of cardiovascular risk factors, is known as obesity cardiomyopathy [26]. Recent studies have shown that there is a rise in the prevalence of heart failure with preserved ejection fraction(HFpEF) among obese people, as excess fat provokes inflammation and is a chief factor in the pathophysiology of HFpEF [49]. Interruption of structural, functional, and electrical physiology of the heart in long-standing obese individuals, irrespective of cardiovascular risk factors, is known as obesity cardiomyopathy [26].

Pathophysiological Mechanisms

When excess fat is present in the body, it accumulates in the heart, which is called epicardial fat. Fat is active at the cellular level and secretes molecules that can promote inflammation. It includes monocyte chemoattractant protein, leptin, resistin, and Tumor necrosis factor-alpha. The chemoattractant protein recruits more M1 macrophages derived from monocytes and induces inflammation and hypertrophy of the left ventricle [50]. Levels of reactive oxygen species are increased due to a lack of proper balance between glucose and fatty acid oxidation. These oxygen radicals result in oxidative stress and interrupt the L-type calcium channels, disturbing the calcium equilibrium and resulting in arrhythmia, especially atrial fibrillation [51]. Neurohormonal changes may result in the release of cytokines called leptin and Tumor necrosis factor-alpha, activating the renin-angiotensin-aldosterone system(RAAS). This activation increases the levels of angiotensin-2 and angiotensin-2 type-1 receptors and their interaction. A pro-fibrotic cytokine, Tumor growth factor-beta, is expressed and leads to myocardial fibrosis by depositing type-1 collagen [52].

Clinical Manifestations

Dyspnea during sleep and physical activity, exhaustion, and cor pulmonale symptoms, such as liver enlargement, distended jugular vein, and swollen extremities, are some of the manifestations of obesity cardiomyopathy [53]. In obese patients, echocardiography falsely indicates pericardial effusion because of the epicardial adipose tissue. Tissue Doppler helps assess the diastolic dysfunction of the left ventricle [54]. One of the imaging tests used to rule out coronary artery disease is positron emission tomography, which is used to check the integrity of the tissue, and another test is single photon emission computed tomography(SPECT). These tests are performed after stressing the cardiac tissue. Among these tests, SPECT gives a much less accurate image when compared to other tests because of the artifacts formed by fat [55].

Section 9: Arrhythmias and Sudden Cardiac Death

Prevalence of Arrhythmias in Obesity

AF is the type of arrhythmia that is most commonly identified among obese patients. Recently, numerous studies have been carried out to understand the link between AF and excess weight. According to recent evidence, each unit's rise in body mass index has shown a 4% rise in the risk of AF. At the same time, a 12% reduction in the chances of AF is shown for every 5-kilogram weight loss [56,57]. According to recent evidence, there is an increased likelihood of metabolic syndrome among obese people, which is characterized by the pathological elevation of serum lipids, high glucose levels, resistance to insulin, and diabetes type-2. Metabolic syndrome and Obesity together can lead to ventricular arrhythmias by modifying the anatomy and physiology of cardiac structure. The exact pathogenesis is not well understood, but some studies have shown it is due to alterations of ion channels of the heart, mainly calcium channel function [58].

Mechanistic Insights

The fat around the heart grows as Obesity increases. This fat is metabolically active and releases various mediators that can modulate the electrophysiological changes by altering L-type calcium channels, gap junctions, and oxidative stress caused by increased reactive oxygen species, slowing the conduction system due to fibrotic tissue buildup in the myocardium. Therefore, this restructuring can increase the formation of arrhythmias(i.e., arrhythmogenesis). However, the accurate pathway is still being explored [59-61]. Excess epicardial fat also disrupts the autonomic nervous system by stimulating the sympathetic nervous system, as it is the source of catecholamines, especially norepinephrine, thereby increasing arrhythmogenesis [62].

Risk of Sudden Cardiac Death

Among various factors, Obesity is a standalone element leading to SCD and arrhythmogenesis. Emerging studies have shown that 23% of patients with obesity cardiomyopathy are associated with sudden cardiac death(SCD). Pathophysiology of SCD involves abnormal events in obese individuals, like the reconfiguration of cardiac structure, particularly hypertrophy of ventricles, fibrosis, and changes in electrophysiology and the autonomic system. Other risk factors may include QT prolongation, nonalcoholic fatty liver disease, and sleep apnea [62]. Oxidative stress drives the Pathogenesis of SCD in sleep apnea [63]. QT prolongation can be caused by antipsychotic drugs that disrupt cardiac physiology [64].

Section 10: Therapeutic Strategies

Lifestyle Interventions

Recent research efforts proved that self-care practices, such as physical training, diet, and weight reduction, tend to improve cardiac activity by reducing inflammation, myocardial thickening, and the

effects of oxygen radicals. A major benefit of excess weight loss is the reduction of QT prolongation via normalizing the physiology of the heart and eventually lowering the risk of AF. Weight loss generally reduces body fat, whereas exercise precisely concentrates on the adiposity around the heart and lowers fat, starting from 5% to 32% [64,65].

Pharmacological Treatments

Drug-based interventions include anti-diabetic drugs, specifically sodium-glucose co-transporter inhibitors (SGLT2 inhibitors), glucagon-like peptides (GLP-1), and statins. Statins like atorvastatin have been used to decrease inflammatory elements and cardiac adiposity. GLP-1 and SGLT2 inhibitors are clinically acceptable options for weight management. SGLT2 inhibitors diminish the risk of arrhythmias by improving abnormal calcium levels and consequently reduce the risk of heart-related deaths. However, its mechanism of action on cardiac tissue is still being explored as heart myocytes do not express SGLT2. Semaglutide is a GLP-1 receptor agonist that helps in 17% weight loss in obese individuals. Meanwhile, GLP-1 Substitute Liraglutide has caused about 40% of epicardial adipose tissue loss. Finally, diuretics and aldosterone agonists are also helpful in altering the structural and electrophysiological abnormalities of the heart [64-66]. **Table 2** provides an overview of the main pharmacological therapies targeting obesity-related cardiovascular risk, detailing each drug class's mechanism of action and its associated cardiovascular benefits.

Table 2. Pharmacological Therapies Targeting Obesity-Related Cardiovascular Risk

Therapy Class	Mechanism of Action	Cardiovascular Benefits	References
GLP-1 agonists	Enhance satiety, improves insulin sensitivity	Weight loss, reduced HFpEF risk	[64,65,66]
SGLT2 inhibitors	Promotes glycosuria, reduces cardiac load	Decreases Heart Failure Hospitalisation, Decreased arrhythmias	[37,64]
PPARγ agonists	Improves adipocyte differentiation	Increased adiponectin, Decreased inflammatory cytokines	[12]
Statins	Inhibits cholesterol synthesis	Decreased LDL-C, Decreased cardiac adiposity	[38,64]

Conclusion

Obesity and metabolic syndrome are a pandemic and new alarming world health problem, which is causally related to cardiovascular morbidity and mortality with complex pathophysiological

mechanisms. In this review, we provide an overview of the accumulating evidence that links the combination of adipose tissue pathology, chronic inflammation, insulin resistance, and ectopic lipid accumulation, underpinning hemodynamic stress, endothelial dysfunction, and structural cardiac disease that leads to heart failure, arrhythmia, and atherosclerosis. Notably, the interaction of neurohormonal activation, lipotoxicity, and adipokine dysregulation highlights the necessity of early, focused interventions to break this harmful cascade.

Novel treatment approaches, such as lifestyle intervention, GLP-1 agonists, and SGLT2 inhibitors, are promising in reducing cardiovascular risk and targeting metabolic derangements and cardiac damage. On the other hand, the increasing incidence of obesity-associated cardiomyopathy and HFpEF may require us to step back and take a new approach to addressing metabolic and cardiovascular health management in an integrated, multilevel, cross-species, multidisciplinary format. Screening for subclinical myocardial injury in obese populations should be a priority for clinicians, and policymakers should promote system-wide interventions aimed at arresting the obesity epidemic with prevention, education, and timely access to emerging interventions.

Future research needs to clarify the molecular mechanisms involved in the crosstalk between the adipose organ and the heart and improve biomarkers for early risk stratification. By integrating mechanistic advances with translational innovation, this review emphasizes the pressing need to re-conceptualize our knowledge of obesity-related cardiovascular disease into clinically and public health actionable solutions.

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აბსტრაქტი:

სიმსუქნე და მეტაბოლური სინდრომი საზოგადოებრივი ჯანდაცვის მნიშვნელოვან პრობლემად იქცა, რამაც გულ-სისხლძარღვთა დაავადებებით გამოწვეული ავადობისა და სიკვდილიანობის მაჩვენებლების ზრდა გამოიწვია. ეს ნარატიული მიმოხილვა წარმოადგენს უახლესი მტკიცებულებების (2017–2024) მიმოხილვას, რათა განაახლოს ძირითადი პათოფიზიოლოგიური დისკუსია ცხიმოვანი ქსოვილის დისფუნქციას, ქრონიკულ ანთებას, ინსულინრეზისტენტობასა და ექტოპიურ ლიპიდურ დეპონირებას შორის ურთიერთკავშირზე, რაც იწვევს ჰემოდინამიკური სტრესის, ენდოთელური დისფუნქციის და გულის სტრუქტურული რემოდელირების განვითარებას. ცენტრალური პათოფიზიოლოგიური დარღვევები მოიცავს ადიპოკინის დისფუნქციას, ცერამიდებისა და დიაცილგლიცეროლების ლიპოტოქსიურ დაზიანებას და რენინ-ანგიოტენზინ-ალდოსტერონისა და სიმპათიკური ნერვული სისტემების ნეიროჰორმონალურ აქტივაციას. ეს პროცესები იწვევს გულ-სისხლძარღვთა ფენოტიპების მრავალფეროვნებას, როგორიცაა გულის უკმარისობა შენარჩუნებული განდევნის ფრაქციით (HFpEF), არითმიები, ათეროსკლეროზი და უეცარი გულის სიკვდილი. კლინიკური თვალსაზრისით, სიმსუქნე ზრდის დიაგნოსტიკურ სირთულეებს ეპიკარდიული ცხიმის ვიზუალიზაციის არტეფაქტებისა და HFpEF-ის გადაფარვის სიმპტომების გამო, ამიტომ საჭიროა მოწინავე ბიომარკერები და ინდივიდუალური დიაგნოსტიკური მეთოდები. ახალი მიდგომები (ცხოვრების წესის ჩარევა, ანტიდიაბეტური პრეპარატები, როგორიცაა SGLT2 ინჰიბიტორები, GLP-1 აგონისტები და ბარიატრიული ქირურგია) ეფექტურად ამცირებს გულ-სისხლძარღვთა რისკს მეტაბოლურ დარღვევებზე, ანთებასა და გულის ადაპტაციაზე მოქმედებით. მიმოხილვა მიუთითებს მრავალმხრივი მოვლის მიწოდების მოდელების საჭიროებაზე, რათა ინტეგრირებული იყოს მეტაბოლური და გულ-სისხლძარღვთა რისკების მართვა და საზოგადოებრივი ჯანდაცვის ძალისხმევის აუცილებლობაზე, რათა შეჩერდეს სიმსუქნის ტალღა და უზრუნველყოფილი იყოს თერაპიაზე თანაბარი წვდომა. მომავალი კვლევები უნდა ფოკუსირებული იყოს ცხიმოვან და ორგანოთა სისტემების დონეებს შორის ურთიერთკავშირის მოლეკულურ მექანიზმებზე და გააუმჯობესოს რისკის სტრატიფიკაციის ინსტრუმენტები სიმსუქნესთან დაკავშირებული გულ-სისხლძარღვთა დაავადებების მიმდინარე ზავის წინააღმდეგ საბრძოლველად.

საკვანძო სიტყვები: სიმსუქნით გამოწვეული კარდიომიოპათია, ინსულინრეზისტენტობა, ადიპოკინები, SGLT2 ინჰიბიტორები, HFpEF.